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The Effect of Calendarized Drug Package on Patients Compliance with Antibiotics

ABSTRACT:

Background: Patients' compliance with antibiotics has been one of the global challenges in combating antibiotics resistance. Patients will tend to forget their antibiotics, especially when they feel better. Related to this phenomenon, the development of medication reminder media is essential. **Aim :** This experimental study was aimed to develop and apply calendarized package as a medication reminder media in patients with short-course antibiotics to improve their compliance.

Methods: Calendarized package was prepared from the labeling of the original package of antibiotics with stickers. Patients above 18 years old who were prescribed short-course oral antibiotics (not more than seven days) during the study period were asked to participate in this study. Patients were grouped into two groups (control and intervention group). Patients' demographical data, medications prescribed, and the last antibiotics course day was recorded. Patients were then contacted for compliance evaluation on the latest antibiotics course day. **Results :** A total of 150 patients who met the inclusion criteria were recruited in this study. 76 patients were grouped into the intervention group, while the remaining 74 patients were the control group. The results showed that the number of compliant patients in the intervention group was higher (72.37%) than those in the control group (45.95%), respectively (p -value <0.000). **Conclusion:** The application of the calendar on the package indicates the positive impact on the patients' compliance with antibiotics. However, in this study, the compliance measurement was conducted indirectly because of the Covid-19 pandemic. However, several limitations should be considered. Future research using a bigger sample size and stricter compliance measurement method is needed to confirm this finding.

KEYWORDS: Calendarized package, Compliance, Antibiotics, Pill count, Community health center.

INTRODUCTION:

Recently, the infectious disease still has a huge contribution to global deaths with 3,2 million mortality rates for lower respiratory tract infection and 1,4 million mortality rates for tuberculosis [1]. However, irrational and overuse of antibiotics can lead to the rise of bacterial resistance. Global Antimicrobial Surveillance System (GLASS) held by World Health Organization (WHO) stated that 500.000 people from 22 countries are exposed to bacterial resistance [2]. The increase of bacterial resistance has consequences to the excess of severity, morbidity, complication, and prolonged hospital stay [3]. One factor related to irrational antibiotics use is patients compliance [4].

Patients' compliance with antibiotics has been one of the global challenges in combating antibiotics resistance. Many factors like forgetting and being too busy have been confirmed as causes of non-compliance [5]. Patients will tend to forget their antibiotics, especially when they feel better. Related to this phenomenon, the development of medication reminder media is essential. Several medication

reminders have been applied in patients with a degenerative disease like a calendarized blister, medication chart, pillbox, diary book, etc [6–9]. Calendarized blister was successful in increasing the compliance and persistence in patients with hypertension. Moreover, medication charts, pillboxes, and diary books have been confirmed can help to improve compliance with patients with hypertension. As far as observed, there is still a lack of data in applying medication reminder media for improving compliance in patients receiving antibiotics. Some studies implemented counseling and education to improve patients' compliance with antibiotics, and the results were variative [10,11]. Therefore, this study was designed to develop and apply calendarized package as a medication reminder media in patients with short-course antibiotics to improve their compliance.

MATERIALS AND METHODS:

Materials

Calendarized package

Calendarized package was prepared from the labeling of the original package of antibiotics with stickers. The stickers were designed for seven days (written in Bahasa Indonesia) and five different times printed in different colors (Table 1). The stickers were applied to the original antibiotics package manually based on patients' prescriptions. Time stickers for antibiotics prescribed three times a day were set at 05.00, 13.00, and 21.00, while for antibiotics prescribed two times a day, the stickers were set at 06.00 and 18.00. For example, if patients are prescribed amoxicillin three times a day on Wednesday, subsequently, stickers will start on Wednesday and end on Saturday (Figure 1).

Table 1. Stickers design

Days (in Indonesian)	Days (in English)	Sticker Design	Times	Sticker Design
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Kamis	Thursday	Kamis	18.00	18.00
Jum'at	Friday	Jumat	21.00	21.00
Sabtu	Saturday	Sabtu		
Minggu	Sunday	Minggu		

Figure 1. Stickers application on antibiotics package



Methods

Study design

This was an experimental study conducted at four community health center in Surabaya (Puskesmas Wonokromo, Puskesmas Kalirungkut, Puskesmas Gayungan, and Puskesmas Kedurus) from January to April 2021. The ethical approval was obtained from the Ethics Committee of Universitas Surabaya. Patients above 18 years old who were prescribed short-course oral antibiotics (not more than seven days) during the study period were asked to participate in this study. Patients who agreed to participate would be asked to sign the informed consent and then classified into two groups using systematic random sampling. Patients who came first, third, fifth (odd number) were grouped into the control group, while those who arrived at second, fourth, sixth (even number) were grouped into the intervention group. We did not interfere with the antibiotics prescription both in the intervention and control group. We calendarized the antibiotics package in the intervention group with the stickers while the control group received medication as a standard operational procedure at the community health center. Patients' demographical data, medications prescribed, and the last antibiotics course day was recorded. Patients were then contacted for compliance evaluation on the latest antibiotics course day.

Compliance measurements

Compliance measurements were conducted using the pill count method. Patients would be considered compliant if the remaining tablets counted not more than 15% of the total tablet prescribed [1]. However, because of the Covid-19 pandemic, the counting process could not be conducted directly. Therefore, we contacted patients on the last antibiotics course day and asked them to fill the online form and upload their remaining tablet pictures.

Data analysis

Baseline characteristic data such as the age, gender, educational background, and the average of drugs consumed were compared between two groups to confirm that there were no differences in the factors that affected compliance. The number of compliant and non-compliant patients in both groups was analyzed using the Chi-square test. P -value $<0,05$ was considered statistically significant in the effect of the calendarized package on the patients' compliance with oral antibiotics.

RESULT:

Baseline Characteristics

A total of 150 patients who met the inclusion criteria were recruited in this study. 76 patients were grouped into the intervention group, while the remaining 74 patients were the control group. All of the patients who joined in this study were received single short course antibiotics. The baseline characteristics of all patients were

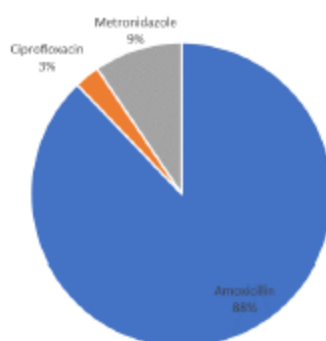
presented in Table 1, and the profile of antibiotics prescribed was illustrated in Figure 1.

Table 1. Baseline Characteristics

Characteristics	Intervention Group	Control Group	p-value
	N = 76	N = 74	
Age**			
<40	61 (53.20)	44 (51.80)	0.005a
≥40	15 (22.80)	30 (22.20)	
Gender**			
Female	50 (65.79)	42 (56.76)	0.937a
Male	26 (34.21)	32 (43.24)	
Education**			
Higher Education	28 (36.84)	21 (28.38)	0.866a
Non-Higher Education	48 (63.16)	53 (71.62)	
Number of drug consumed*	3.70 ± 1.03	3.60 ± 1.00	0.269b

*Data presented in Average±SD; **Data presented in n(%); aChi-square test; bIndependent T-Test

Table 1 shows that there was no difference between the average number of drugs consumed and the distribution of gender and educational background (p-value >0.05). However, in the distribution of age, there was a significant difference between the two groups (p-value <0.05).



(a)

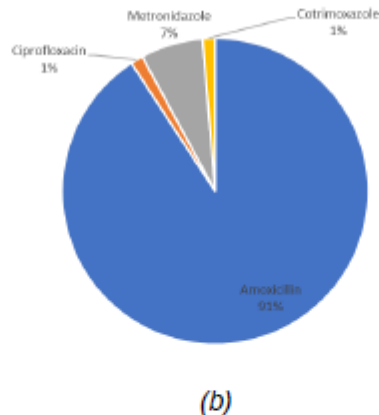


Figure 1. (a) Antibiotics Prescribed in Control Group; (b) Antibiotics Prescribed in Intervention Group

Figure 1 shows that both in the control and intervention groups, the most frequently prescribed antibiotic was amoxicillin with a dosage of 500 mg three times a day. The other antibiotics prescribed were metronidazole 500 mg three times a day, ciprofloxacin 500 mg two to three times a day, and cotrimoxazole 960 mg two times a day.

Patients Compliance

Patients' compliance was measured by counting the remaining antibiotics in the last day course. The distribution of compliance patients in both groups was presented in Table 2 below. The Analysis results demonstrated that the p -value was <0.005 . Consequently, the number of compliance patients between the two groups compared was statistically significant.

Table 2. Patients Compliance with Antibiotics

Groups	Compliance	Non-Compliance	p -value
Intervention Group N = 76	55 (72.37)	21 (27.63)	0.002a
Control Group N = 74	34 (45.95)	40 (54.05)	

*Data presented in Average \pm SD; **Data presented in n(%); aChi-square test

DISCUSSION:

Compliance is one of the concerns in controlling the rise of bacterial resistance. In addition, non-compliance with antibiotics therapy may also lead to therapeutic failure and reinfection [13]. Increasing antibiotics compliance will have a positive impact on treatment outcomes and also suppress bacterial resistance. Our analysis results indicated that calendarized package has a potential effect on the patients'

compliance with antibiotics which showed in Table 2. The number of compliant patients in the intervention group was higher than those in the control group. This finding could lead to additional tools in antibiotics prescription service. Day and time administration schedule on the packaging would help patients remember their antibiotics dosage and improve compliance.

As far as our observation, the concept of reminder packaging has not been applied to improving antibiotics compliance before. However, reminder or calendarized packaging has been confirmed on the improving of hypertensive patients' compliance. A previous study by Dupclay et al. stated that the use of reminder packaging had a positive role in consistent improvement in adherence and persistence of patients on an antihypertensive regimen [7]. Reminder or calendarized packaging might be a helpful tool for patients who likely to forget their therapeutics dosage. A study by Schneider et al. showed that daily dose blister packaging (pill-calendar) helped elderly patients remember their medication. It was proved by their higher medication possession ratios ($P = 0.04$) and lower diastolic blood pressure ($P = 0.01$) than patients who used traditional bottles [14]. The same reason might underlie the results of this study. Patients receiving antibiotics often miss their dosage because of simply forgetting [15].

The findings in this study indicate a potential role of the calendarized package in improving patients compliance. However, this study has several limitations that should be considered. The first limitation is in the distribution of patients' age recruited between two groups. The analysis results in Table 1 showed a significant difference in patients' age which can intervene in patients' compliance. Age was confirmed as the independent factor related to nonadherence. Poor compliance in older age, especially the elderly, is associated with the decline in memory, forgetfulness, which was influenced by advertisements and the preference for secret recipes or food therapy [4,13,16]. Bigger sample size in further study is needed to minimize the bias caused by the different age profiles between the two groups. In addition, because of pandemic Covid-19, the compliance measurement was conducted indirectly. Therefore, future research using stricter compliance measurement methods is needed to confirm this finding.

CONCLUSION:

The application of the calendar on the package indicates the positive impact on the patients' compliance with antibiotics. However, several limitations should be considered. Future research using a bigger sample size and stricter compliance measurement method is needed to confirm this finding.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation.

ACKNOWLEDGMENTS:

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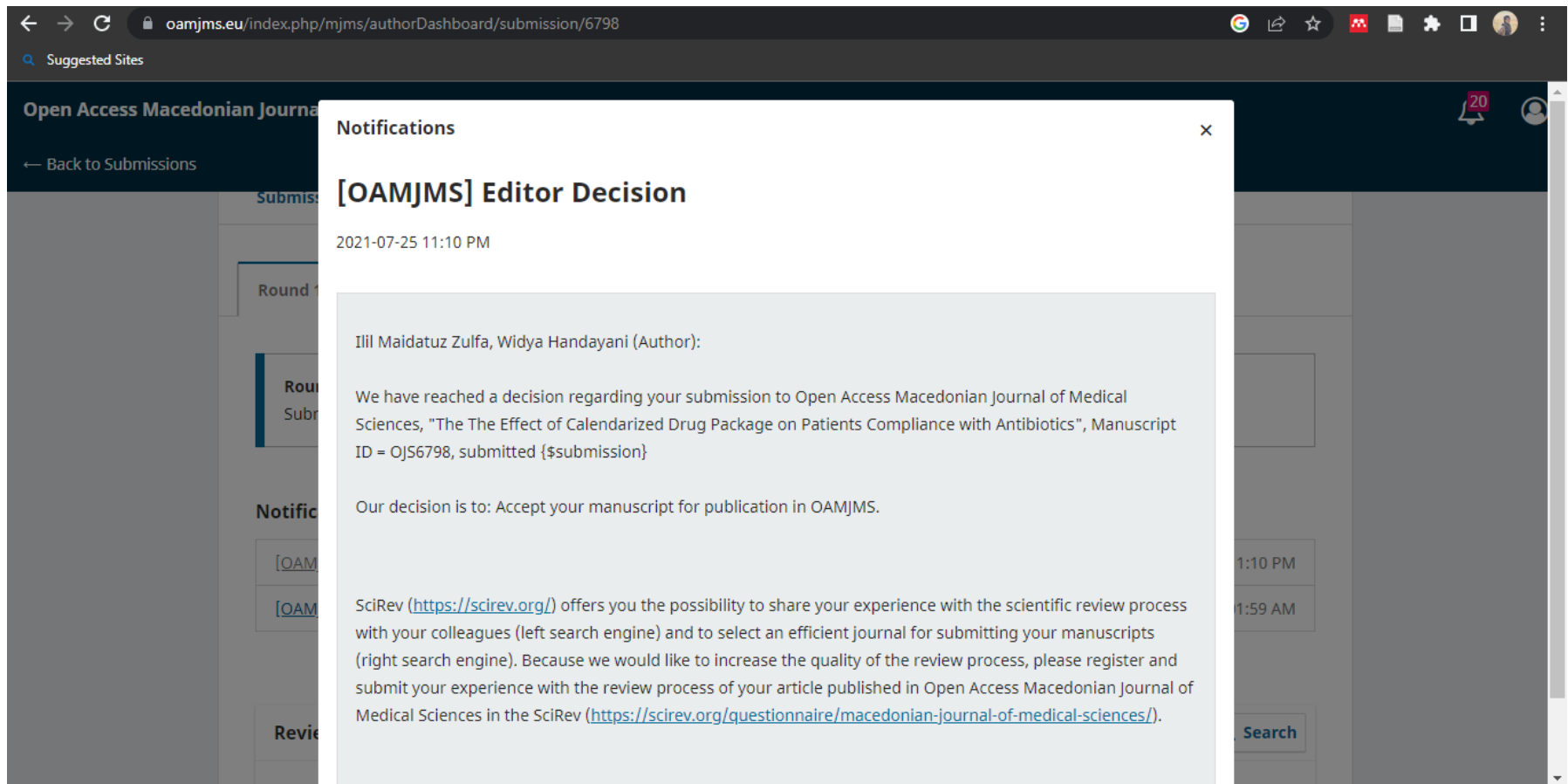
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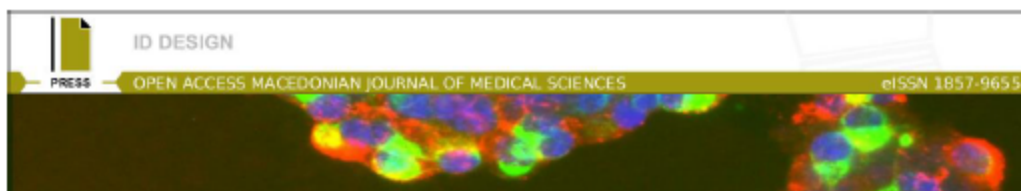
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The Effect of Calendarized Drug Package on Patients Compliance with Antibiotics

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Abstract

BACKGROUND: Patients' compliance with antibiotics has been one of the global challenges in combating antibiotics resistance. Patients will tend to forget their antibiotics, especially when they feel better. Related to this phenomenon, the development of medication reminder media is essential.

AIM: This experimental study was aimed to develop and apply calendarized package as a medication reminder media in patients with short-course antibiotics to improve their compliance.

METHODS: Calendarized package was prepared from the labeling of the original package of antibiotics with stickers. Patients above 18 years old who were prescribed short-course oral antibiotics (not more than 7 days) during the study period were asked to participate in this study. Patients were grouped into two groups (control and intervention group). Patients' demographical data, medications prescribed, and the last antibiotics course day was recorded. Patients were then contacted for compliance evaluation on the latest antibiotics course day.

RESULTS: A total of 150 patients who met the inclusion criteria were recruited in this study. Seventy-six patients were grouped into the intervention group, while the remaining 74 patients were the control group. The results showed that the number of compliant patients in the intervention group was higher (72.37%) than those in the control group (45.95%), respectively ($p < 0.000$).

CONCLUSION: The application of the calendar on the package indicates the positive impact on the patients' compliance with antibiotics. However, in this study, the compliance measurement was conducted indirectly because of the coronavirus disease 2019 pandemic. However, several limitations should be considered. Future research using a bigger sample size and stricter compliance measurement method is needed to confirm this finding.

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Keywords: Calendarized package, Compliance, Antibiotics, Pill count, Community health center
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Introduction

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Data analysis

Baseline characteristic data such as the age, gender, educational background, and the average of drugs consumed were compared between two groups to confirm that there were no differences in



Figure 1: Stickers application on antibiotics package

the factors that affected compliance. The number of compliant and non-compliant patients in both groups was analyzed using the Chi-square test. $p < 0,05$ was considered statistically significant in the effect of the calendarized package on the patients' compliance with oral antibiotics.

Results

Baseline characteristics

A total of 150 patients who met the inclusion criteria were recruited in this study. Seventy-six patients were grouped into the intervention group, while the remaining 74 patients were the control group. All of the patients who joined in this study were received single short course antibiotics. The baseline characteristics of all patients were presented in Table 2, and the profile of antibiotics prescribed was illustrated in Figure 1.

Table 2: Baseline Characteristics

Characteristics	Intervention Group n = 76	Control Group n = 74	p-value
Age**			
<40	61 (53.20)	44 (51.80)	0.005*
>40	15 (22.80)	30 (22.20)	
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Number of drug consumed*	3.70 ± 1.03	3.60 ± 1.00	0.269*

*Data presented in Average ± SD; **Data presented in n (%); *Chi-square test; *Independent t-test

Table 2 shows that there was no difference between the average number of drugs consumed and the distribution of gender and educational background ($p > 0.05$). However, in the distribution of age, there was a significant difference between the two groups ($p < 0.05$).

Figure 2 shows that both in the control and intervention groups, the most frequently prescribed antibiotic was amoxicillin with a dosage of 500 mg 3 times a day. The other antibiotics prescribed were metronidazole 500 mg 3 times a day, ciprofloxacin

500 mg 2 to 3 times a day, and cotrimoxazole 960 mg 2 times a day.

Patients compliance

Patients' compliance was measured by counting the remaining antibiotics in the last day course. The distribution of compliance patients in both groups was presented in Table 3 below. The Analysis results demonstrated that the $p < 0.005$. Consequently, the number of compliance patients between the two groups compared was statistically significant.

Table 3: Patients Compliance with Antibiotics

Groups	Compliance	Non-compliance	p-value
Intervention Group n = 76	65 (72.37)	21 (27.63)	0.002*
Control Group n = 74	34 (45.95)	40 (54.05)	

*Data presented in Average ± SD; **Data presented in n (%); *Chi-square test.

Discussion

Compliance is one of the concerns in controlling the rise of bacterial resistance. In addition, non-compliant with antibiotics therapy may also lead to therapeutic failure and reinfection [13]. Increasing antibiotics compliance will have a positive impact on treatment outcomes and also suppress bacterial resistance. Our analysis results indicated that calendarized package has a potential effect on the patients' compliance with antibiotics which showed in Table 3. The number of compliant patients in the intervention group was higher than those in the control group. This finding could lead to additional tools in antibiotics prescription service. Day and time administration schedule on the packaging would help patients remember their antibiotics dosage and improve compliance.

As far as our observation, the concept of reminder packaging has not been applied to improving antibiotics compliance before. However, reminder or calendarized packaging has been confirmed on the improving of hypertensive patients' compliance. A previous study by Dupclay *et al.* stated that the use of reminder packaging had a positive role in consistent improvement in adherence and persistence of patients on an antihypertensive regimen [7]. Reminder or calendarized packaging might be a helpful tool for patients who likely to forget their therapeutics dosage. A study by Schneider *et al.* showed that daily dose blister packaging (pill-calendar) helped elderly patients remember their medication. It was proved by their higher medication possession ratios ($p = 0.04$) and lower diastolic blood pressure ($p = 0.01$) than patients who used traditional bottles [14]. The same reason might underlie the results of this study. Patients receiving antibiotics often miss their dosage because of simply forgetting [15].

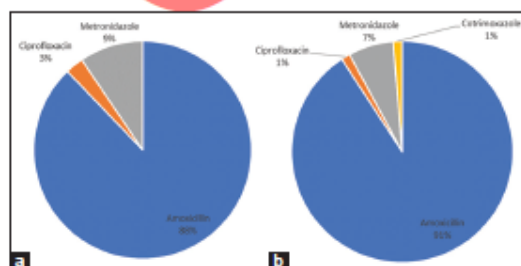


Figure 2: (a) Antibiotics prescribed in control group; (b) Antibiotics prescribed in intervention group

The findings in this study indicate a potential role of the calendarized package in improving patients compliance. However, this study has several limitations that should be considered. The first limitation is in the distribution of patients' age recruited between two groups. The analysis results in Table 2 showed a significant difference in patients' age which can intervene in patients' compliance. Age was confirmed as the independent factor related to nonadherence. Poor compliance in older age, especially the elderly, is associated with the decline in memory, forgetfulness, which was influenced by advertisements and the preference for secret recipes or food therapy [4], [13], [16]. Bigger sample size in further study is needed to minimize the bias caused by the different age profiles between the two groups. In addition, because of the pandemic COVID-19, the compliance measurement was conducted indirectly. Therefore, future research using stricter compliance measurement methods is needed to confirm this finding.

Conclusion

The application of the calendar on the package indicates the positive impact on the patients' compliance with antibiotics. However, several limitations should be considered. Future research using a bigger sample size and stricter compliance measurement method is needed to confirm this finding.

Acknowledgments

The authors would like to thank The Ministry of Research and Technology/National Agency for Research and Innovation of Indonesia (Kemristekdikti) for the funding support in the scheme of National Competitive National Research and all the community health centers personnel for the research permission.

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5. Paper published (09 September 2021)

Published Article



The Effect of Calendarized Drug Package on Patients Compliance with Antibiotics

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Abstract

BACKGROUND: Patients' compliance with antibiotics has been one of the global challenges in combating antibiotics resistance. Patients will tend to forget their antibiotics, especially when they feel better. Related to this phenomenon, the development of medication reminder media is essential.

AIM: This experimental study was aimed to develop and apply calendarized package as a medication reminder media in patients with short-course antibiotics to improve their compliance.

METHODS: Calendarized package was prepared from the labeling of the original package of antibiotics with stickers. Patients above 18 years old who were prescribed short-course oral antibiotics (not more than 7 days) during the study period were asked to participate in this study. Patients were grouped into two groups (control and intervention group). Patients' demographical data, medications prescribed, and the last antibiotics course day was recorded. Patients were then contacted for compliance evaluation on the latest antibiotics course day.

RESULTS: A total of 150 patients who met the inclusion criteria were recruited in this study. Seventy-six patients were grouped into the intervention group, while the remaining 74 patients were the control group. The results showed that the number of compliant patients in the intervention group was higher (72.37%) than those in the control group (45.95%), respectively ($p < 0.000$).

CONCLUSION: The application of the calendar on the package indicates the positive impact on the patients' compliance with antibiotics. However, in this study, the compliance measurement was conducted indirectly because of the coronavirus disease 2019 pandemic. However, several limitations should be considered. Future research using a bigger sample size and stricter compliance measurement method is needed to confirm this finding.

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Introduction

Recently, the infectious disease still has a huge contribution to global deaths with 3.2 million mortality rates for lower respiratory tract infection and 1.4 million mortality rates for tuberculosis [1]. However, irrational and overuse of antibiotics can lead to the rise of bacterial resistance. Global Antimicrobial Surveillance System held by the World Health Organization stated that 500,000 people from 22 countries are exposed to bacterial resistance [2]. The increase of bacterial resistance has consequences to the excess of severity, morbidity, complication, and prolonged hospital stay [3]. One factor related to irrational antibiotics use is patients compliance [4].

Patients' compliance with antibiotics has been one of the global challenges in combating antibiotics resistance. Many factors such as forgetting and being too busy have been confirmed as causes of non-compliance [5]. Patients will tend to forget their antibiotics, especially when

they feel better. Related to this phenomenon, the development of medication reminder media is essential. Several medication reminders have been applied in patients with a degenerative disease such as a calendarized blister, medication chart, pillbox, diary book. [6], [7], [8], [9]. Calendarized blister was successful in increasing the compliance and persistence in patients with hypertension. Moreover, medication charts, pillboxes, and diary books have been confirmed can help to improve compliance with patients with hypertension.

As far as observed, there is still a lack of data in applying medication reminder media for improving compliance in patients receiving antibiotics. Some studies implemented counseling and education to improve patients' compliance with antibiotics, and the results were variative [10], [11]. Therefore, this study was designed to develop and apply calendarized package as a medication reminder media in patients with short-course antibiotics to improve their compliance.

Materials and Methods

Materials

Calendarized package

Calendarized package was prepared from the labeling of the original package of antibiotics with stickers. The stickers were designed for 7 days (written in Bahasa Indonesia) and five different times printed in different colors (Table 1). The stickers were applied to the original antibiotics package manually based on patients' prescriptions. Time stickers for antibiotics prescribed 3 times a day were set at 05.00, 13.00, and 21.00, while for antibiotics prescribed 2 times a day, the stickers were set at 06.00 and 18.00. For example, if patients are prescribed amoxicillin 3 times a day on Wednesday, subsequently, stickers will start on Wednesday and end on Saturday (Figure 1).

Table 1: Stickers design

Days (in Indonesian)	Days (in English)	Sticker Design	Times	Sticker Design
Senin	Monday	Senin	05.00	05.00
Selasa	Tuesday	Selasa	06.00	06.00
Rabu	Wednesday	Rabu	13.00	13.00
Kamis	Thursday	Kamis	18.00	18.00
Jum'at	Friday	Jumat	21.00	21.00
Sabtu	Saturday	Sabtu		
Minggu	Sunday	Minggu		

Methods

Study design

This was an experimental study conducted at four community health center in Surabaya (Puskesmas

Wonokromo, Puskesmas Kalirungkut, Puskesmas Gayungan, and Puskesmas Kedurus) from January to April 2021. The ethical approval was obtained from the Ethics Committee of Universitas Surabaya. Patients above 18 years old who were prescribed short-course oral antibiotics (not more than 7 days) during the study period were asked to participate in this study. Patients who agreed to participate would be asked to sign the informed consent and then classified into two groups using systematic random sampling. Patients who came first, third, fifth (odd number) were grouped into the control group, while those who arrived at second, fourth, and sixth (even number) were grouped into the intervention group. We did not interfere with the antibiotics prescription both in the intervention and control group. We calendarized the antibiotics package in the intervention group with the stickers while the control group received medication as a standard operational procedure at the community health center. Patients' demographical data, medications prescribed, and the last antibiotics course day was recorded. Patients were then contacted for compliance evaluation on the latest antibiotics course day.

Compliance measurements

Compliance measurements were conducted using the pill count method. Patients would be considered compliant if the remaining tablets counted not more than 15% of the total tablet prescribed [12]. However, because of the coronavirus disease 2019 (COVID-19) pandemic, the counting process could not be conducted directly. Therefore, we contacted patients on the last antibiotics course day and asked them to fill the online form and upload their remaining tablet pictures.

Data analysis

Baseline characteristic data such as the age, gender, educational background, and the average of drugs consumed were compared between two groups to confirm that there were no differences in



Figure 1: Stickers application on antibiotics package

the factors that affected compliance. The number of compliant and non-compliant patients in both groups was analyzed using the Chi-square test. $p < 0,05$ was considered statistically significant in the effect of the calendarized package on the patients' compliance with oral antibiotics.

Results

Baseline characteristics

A total of 150 patients who met the inclusion criteria were recruited in this study. Seventy-six patients were grouped into the intervention group, while the remaining 74 patients were the control group. All of the patients who joined in this study were received single short course antibiotics. The baseline characteristics of all patients were presented in Table 2, and the profile of antibiotics prescribed was illustrated in Figure 1.

Table 2: Baseline Characteristics

Characteristics	Intervention Group <i>n</i> = 76	Control Group <i>n</i> = 74	p-value
Age**			
<40	61 (53.20)	44 (51.80)	0.005*
>40	15 (22.80)	30 (22.20)	
Gender**			
Female	50 (65.79)	42 (56.76)	0.937*
Male	26 (34.21)	32 (43.24)	
Education**			
Higher Education	28 (36.84)	21 (28.38)	0.866*
Non-Higher Education	48 (63.16)	53 (71.62)	
Number of drug consumed*	3.70 ± 1.03	3.60 ± 1.00	0.269 ^b

*Data presented in Average ± SD; **Data presented in n (%); *Chi-square test; ^bIndependent t-test

Table 2 shows that there was no difference between the average number of drugs consumed and the distribution of gender and educational background ($p > 0.05$). However, in the distribution of age, there was a significant difference between the two groups ($p < 0.05$).

Figure 2 shows that both in the control and intervention groups, the most frequently prescribed antibiotic was amoxicillin with a dosage of 500 mg 3 times a day. The other antibiotics prescribed were metronidazole 500 mg 3 times a day, ciprofloxacin

500 mg 2 to 3 times a day, and cotrimoxazole 960 mg 2 times a day.

Patients compliance

Patients' compliance was measured by counting the remaining antibiotics in the last day course. The distribution of compliance patients in both groups was presented in Table 3 below. The Analysis results demonstrated that the $p < 0.005$. Consequently, the number of compliance patients between the two groups compared was statistically significant.

Table 3: Patients Compliance with Antibiotics

Groups	Compliance	Non-compliance	p-value
Intervention Group <i>n</i> = 76	55 (72.37)	21 (27.63)	0.002*
Control Group <i>n</i> = 74	34 (45.95)	40 (54.05)	

*Data presented in Average ± SD; **Data presented in n (%); *Chi-square test.

Discussion

Compliance is one of the concerns in controlling the rise of bacterial resistance. In addition, non-compliant with antibiotics therapy may also lead to therapeutic failure and reinfection [13]. Increasing antibiotics compliance will have a positive impact on treatment outcomes and also suppress bacterial resistance. Our analysis results indicated that calendarized package has a potential effect on the patients' compliance with antibiotics which showed in Table 3. The number of compliant patients in the intervention group was higher than those in the control group. This finding could lead to additional tools in antibiotics prescription service. Day and time administration schedule on the packaging would help patients remember their antibiotics dosage and improve compliance.

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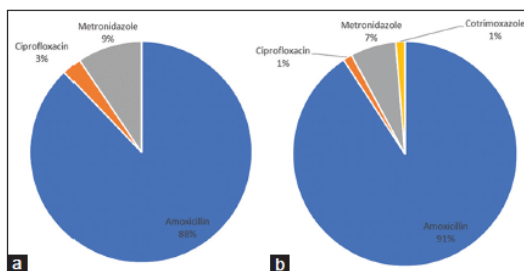


Figure 2: (a) Antibiotics prescribed in control group; (b) Antibiotics prescribed in intervention group

The findings in this study indicate a potential role of the calendarized package in improving patients compliance. However, this study has several limitations that should be considered. The first limitation is in the distribution of patients' age recruited between two groups. The analysis results in Table 2 showed a significant difference in patients' age which can intervene in patients' compliance. Age was confirmed as the independent factor related to nonadherence. Poor compliance in older age, especially the elderly, is associated with the decline in memory, forgetfulness, which was influenced by advertisements and the preference for secret recipes or food therapy [4], [13], [16]. Bigger sample size in further study is needed to minimize the bias caused by the different age profiles between the two groups. In addition, because of the pandemic COVID-19, the compliance measurement was conducted indirectly. Therefore, future research using stricter compliance measurement methods is needed to confirm this finding.

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