Adherence to antibiotics among adults at state sector primary care in a district of Sri Lanka – a descriptive cross sectional study

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(Key words: antibiotic adherence, associated factors, primary care, adults, left over antibiotics)

Abstract

Objectives: To assess the adherence and factors associated with oral antibiotic prescriptions among adults in state sector primary care while assessing the intention to use leftover antibiotics (LOAB).

Methodology: A descriptive cross sectional study was conducted in outpatient departments including 407 adults (18-75) using an interviewer administered questionnaire at consultation and a telephone interview at due completion of antibiotic. Adherence was measured by a self-report supplemented by remaining pill count. Factors associated with adherence were determined. The statistical significance was considered as $p \leq 0.05$.

Results: Adherence to antibiotic prescription was 45.5%. Female gender (p=0.029, OR=1.86) and awareness on the current antibiotic prescription (p=0.000, OR=6.37) were positive associations. Adherence was inversely proportionate to increasing daily dosage frequency (p=0.001). Patient's belief, they can stop medicine once they feel better (p=0.000), fast improvement of symptoms with medication (p=0.000), interference to lifestyle by the antibiotic dosage schedule (p=0.000) and using LOAB in the past (p=0.000,) were negatively associated. Of the non-adherent patients 20.3% intended to use LOAB later.

Conclusions: Adherence to oral antibiotic prescriptions was poor. Patient's gender, patient beliefs and practices towards medicine and complexity of dosage schedule were associated factors. Patient awareness on the current prescription promoted adherence. Intension to use LOAB was high.

Recommendations: Primary care prescribers should make patients aware on antibiotic prescriptions while using less complex regimens.

Introduction

Antibiotics are widely used around the world to treat and prevent bacterial infections [1]. Antibiotic resistance (ABR) is a state in which a bacteria once sensitive to a particular antibiotic develops resistant mutations making it less susceptible or no longer sensitive at all [2]. ABR declines treatment efficacy, increases mortality and health costs becoming one of the major threats to universal health [3,4]. The situation is even worse in the Asian region where ABR was found to be a major health hazard further intensified by the poorly developed health infrastructure [5,6].

Medication adherence is defined as the extent to which an individual patient's medication-taking behavior corresponds with the recommendations of the prescriber [7]. Among other causes such as inappropriate antibiotic prescription, overuse and misuse, non-adherence to antibiotic prescriptions by patients had been identified as an important modifiable cause for ABR [8]. Antibiotics remaining from previous non-adherence or leftovers had been identified as a source of self-medication or sharing with others which further aggravates ABR [9].

The burden of ABR on the health sector of Sri Lanka was clearly highlighted by the Sri Lanka College of Microbiologists (SLCM) in the report on "National Surveillance on Antimicrobial Resistance" December 2014 [10]. The rates of ABR in Sri Lanka had shown increasing trends complicated by multi-drug resistance posing a threat to patient safety while increasing the health cost [11]. In order to combat the growing threat of ABR, improving patient adherence to prescribed antibiotics would be a plausible solution. Although, studies had been done in other countries to determine adherence and factors

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associated with adherence to oral antibiotics in patients [12,13,14], research of this nature is lacking in Sri Lanka. As a substantial proportion of antibiotics are prescribed in primary care [15], this study was done at primary care settings to find out the existing level of adherence and associated factors which was not studied before. The findings of this study will be used to develop strategic measures to improve patient adherence to prescribed antibiotics at primary care.

Objectives

Aim of this study was to assess the adherence and to describe the factors associated with adherence to prescribed oral antibiotics in adults presenting to outpatient departments of three selected state sector primary care settings in a district of Sri Lanka. It was further extended to determine the intention to use leftover antibiotics (LOAB) in the non-adherent patients.

Method

Study design, setting and participants

A descriptive cross sectional study with a telephone follow up was conducted. Adult patients from age 18 to 75 years prescribed on oral antibiotics available at outpatient departments of three selected state sector hospitals in the Gampaha district of Sri Lanaka were included. Three study settings were selected out of outpatient departments of two District general hospitals, three A grade divisional hospitals and 45 Primary Medical Care Units governed by the Regional Director of Health Service, Gampaha using computer generated simple random sampling.

As previous data was not available on adherence to antibiotics in adults in the local settings, sample size calculation assumed a 50% prevalence of adherence to achieve appropriate sample size using the following formula.

$$n = \frac{Z_{1-\alpha/2}{}^2 \, P \, (1-P)}{d^2}$$

The sample (n) required to estimate a proportion (p) of 50% with a standard normal deviation with 95% confidence interval ($Z_{1-\alpha/2}$) within ±5% precision (d) was 384. A total of 518 patients were included adding 35% to the minimum sample to cover the anticipated nonresponse rate during the follow-up telephone interview. Systematic sampling using the outpatients' attendance register, was used in sample selection. Patients presented with emergencies, those with hearing or speaking impairment, who needed others' assistance to take medication, and who were on treatment for psychiatric illnesses were excluded from the study. The study obtained approval from the Ethics Review Committee, Postgraduate Institute of Medicine, Colombo, Sri Lanka.

Data collection

Data collection was done over a period of three months from March to May 2019. Following written informed consent from the patients, the first part of data collection was carried out face to face using a pretested structured questionnaire on sociodemographics information, factors related to illness, therapy and the healthcare system. Details of the prescription, names of all the medications including the antibiotic, dosages, number of units delivered, dosing frequency, and duration of treatment were noted. At this point, participants were not informed about the assessment of adherence to antibiotics in order to minimize the influence on actual practice. The second part of data collection was a telephone interview at the end of the antibiotic regimen to assess adherence. Patient self-reported adherence was supplemented by a remaining antibiotic pill count. Pill count of all the remaining medications were obtained to avoid reporting bias. In this study, we defined adherence to antibiotic prescription as zero remaining antibiotic pills at the time of telephone interview.

Statistical analysis

Adherence to antibiotic prescription was the principal outcome measure of the study, and was assessed as a percentage of the study sample. To identify the factors associated with adherence, Pearson Chi-Square test and Fisher's Exact test were used where necessary in a bivariate analysis of categorical and numerical variables. Statistical significance (p) was set at a value ≤0.05. Multivariate analysis was conducted entering variables with p≤0.05 in a binary logistics regression model to eliminate the confounding effect. Odds of associations were estimated with a 95% confidence interval (95% CI). The intention to use LOAB among the non-adherent group was calculated as a percentage.

Results

A final sample of 407 were eligible for analysis. The response rate was 78.5%. The mean age of the sample was 43.4± 15.8 (mean ± standard deviation) years, 52.9% of the sample were females and 92.8% were Sinhalese. More than 80% of the sample were married and living with family or relatives. Out of the sample, 81.3% had entered secondary school. The majority (52.6%) of the sample reported respiratory symptoms and 77.4% were continuing their daily activities in spite of the illness. Antibiotics with three times daily dosing were prescribed in the majority (70.8%). Regarding patient beliefs about medication, 57.5% believed medication can be stopped once they feel better. At the consultation, 17% were explained on the reason for prescription and 8.4% received instructions on medication administration by the prescriber. Only 10.1% were aware about their antibiotic prescription. Of the sample 17.9% reported using LOAB in the past (Table 1).

Adherence to antibiotic prescription in the sample was 45.5%. The bivariate analysis identified several independent variables being significantly associated with adherence. Female gender (p=0.003), patient awareness on antibiotic prescription (p=0.000), patient belief as the prescribed medication should be completed (p=0.001), the effect of medicine is lost even a single dose is missed (p=0.03) and getting instructions by the prescriber on medication administration (p=0.002) were associated with increasing adherence. Patients believing medication can be stopped once they feel better (p=0,000), fast improvement of symptoms with therapy (p=0.000), daily antibiotic dose frequency more than two times (0.000), dosing frequency interfering with lifestyle (p=0.000) and using LOAB in the past (0.000) were factors increasing the risk of non-adherence. No association was found with age of the patient, ethnicity, marital status, level of education, monthly income, using long term other medication or receiving information regarding medication by the pharmacist.

The multivariate logistics regression model identified (Table 2) female gender (OR=1.8) and awareness about antibiotic prescriptions (OR=6.4) as independent positive detriments of adherence to antibiotic prescription while the same analysis confirmed increasing antibiotic dosing frequency more than two times a day, dosing frequency interfering with lifestyle. Patients believing they can stop medication when they feel better, fast improvement of symptoms with treatment and using LOAB in the past as independent negative determinants of adherence

Seventy-eight non adherent patients (35.1%) had reported symptom improvement as the reason for premature halt of antibiotic regimen being second only to forgetfulness (50.9%) (Table 3). Of the 222 non-adherent patients 20.3% reported to have the intention to keep LOAB from the current regimen for future use (Table 4).

Table 1. Demographics of the study population (n= 407)

	Frequency (n)	%
Aged		
≤45	240	59
>45	167	41
Gender		
Male	166	40.8
Female	241	59.2
Ethnicity		
Sinhalese	377	92.6
Others*	30	7.4
Marital status		
Married	388	83
Single/divorced/widowed	69	17
Level of education		
Below secondary	76	18.7
Secondary and above	331	81.3
Employment status		
Currently employed	208	51.1
Currently not employed	199	48.9
Monthly income		
≤25,000	131	32.2
>25,000	276	67.8

* Tamils, Muslims and Burghers

Table 2. Bivariate analysis of factors associated with adherence to antibiotic prescription

Variable	Adhered n=185	Non adhered n=222	P	OR	95% CI
	n(%)	n(%)			
Gender					
Male	61 (36.7)	103 (63.3)	0.02	1.86	0.366-0.821
Female	124 (51.5)	117 (48.5)			
Can stop when better[a]					
Yes	43 (24.9)	130 (75.1)	<0.001	0.227	0.139-0.331
No	142 (60.7)	92 (39.3)			
Should be completed					
Yes	144 (50.7)	140 (49.3)	0.001	0.486	0.313-0.756
No	41 (33.3)	82 (66.7)			
Speed of improvement[b]					
Fast	16 (12.2)	115 (87.8)	<0.001	0.092	0.052-0.165
Slow/ no improvement	169 (61.2)	107 (38.8)			
Antibiotic dosing frequency					
2	43 (79.6)	11 (20.4)	0.001	0.220	2.89-11.645
>2	142 (40.2)	211 (59.8)			
Interference to lifestyle[c]					
Yes	8 (14.3)	48 (85.7)	<0.001	0.106	0.075-0.356
No	175 (46.5)	174 (49.6)			
Awareness on current antibiotic[d]					
Yes	32 (82.9)	7 (17.1)	0.000	6.378	2.987-16.014
No	151 (41.3)	215 (58.7)			
Instructions by the doctor					
Yes	24 (70.6)	10 (29.4)	0.002	0.316	0.147-0.680
No	161 (43.2)	212 (56.8)			
Using LOAB in the past[e]					
Yes	13 (17.8)	60 (82.8)	<0.001	0.229	0.108 - 0.380
No	172 (51.2)	162 (48.5)			

[a] Patient belief on stopping medication when they feel better

[b] Improvement of symptoms with medication

[c] Interference to life style by the antibiotic dosing frequency

[d] Knowing they were going to be on antibiotics before use

[e] Left over antibiotics

p = Statistical significance, OR = odds ratio estimates, 95%CI = 955 confidence interval

Table 3. Patient reported reasons for non-adherence (n=222)

Reason for nonadherence	Frequency	%
Forgetfulness	113	50.9
As symptoms improved	78	35.1
Due to side effects	19	8.5
Dosage schedule interfering with lifestyle	7	3.1
No confidence in treatment	3	1.3
No improvement of symptoms	2	0.9

Table 4. How LOAB were intended to be handled by non-adherent patients (n=222)

Way of handling	Frequency (n=222)	%
Will discard	104	46.8
Will continue using	72	32.4
Will keep for future use	45	20.3
Not yet decided	1	0.5

Discussion

According to the best of our knowledge, this is the first study carried out on adherence to antibiotics among adults in primary care settings of Sri Lanka. It, therefore, adds value to the limited information available. The study found an adherence of 45.5% to antibiotic prescriptions in adults presenting to state-sector primary care. This is compatible with that of the International Primary Care Observational Study by GRACE study group [13] which demonstrated a mean adherence of 44.2% using a combination of adherence measures but was lower than the adherence of 59.3% reported by Carl L *et al.* [16] using patient self-reports alone. The current study finding of 54.5% non-adherence was lower than that of a study done among patients visiting community pharmacies (57.7%) in Lisbon [12] using a telephone interview but higher than the Italian primary care study [17] which reported a non-adherence of 45% using patient self-reports. The differences might be due to the different definitions and measures of adherence and different methodologies. The supplementation of self-report with a remaining pill count had increased the strength of the current study when compared to studies based on patient self-reports as the latter might be liable to social desirability bias.

The study found several independent determinants of adherence to antibiotic prescriptions in the study population. Female gender was found to be a positive determinant of adherence to antibiotic prescription. Previous researches did not find an association of adherence behaviour with the gender of the patient [12,13,14]. Females being the majority of the sample (59.2%), might have influenced the current finding. In this study, 65.6% of females believe that medicine cannot be stopped once they feel better and should complete while only 23.5% of the males do so. The study found the belief in patients, that they can stop medication when they feel better, as a significant negative determinant of their adherence. Pechere JC *et al.* [18] reported a similar finding. According to the present study, using LOAB from previous incomplete regimens significantly reduces adherence to current antibiotic prescriptions. It implies the habitual nature of non-adherent behaviour that should be challenged. The current study found fast improvement of symptoms, to be a factor reducing adherence to prescribed antibiotics in accordance with a study done by Pechere JC [18] showing improvement of symptoms being the second commonest reason for non-adherence next to forgetfulness. A daily antibiotic dosage frequency of more than two times increased the risk of non-adherence as reported by previous authors [12,19]. The current study demonstrated a significant negative association between the interference with patient's lifestyle by the dosage schedule of antibiotic and adherence. The same was established by Yamamoto Y *et al* [20]. The most striking evidence of this study was the highly significant association of adherence to antibiotics with patient's awareness on the current antibiotic prescription. The study showed, knowing they were going to be on antibiotics, increases the odds of adherence by 6.4 folds (OR=6.378). This observation was in line with previous studies on short term antibiotics [21]. The study found 20.3% of the non-adherent patients and 11% of the whole sample having the intention to use LOAB in the future. This percentage was lower than that found in the "Global Survey on Antibiotic Leftovers in Outpatient Settings" which stated that, out of participants who had antibiotic leftovers at home, 77% of them had the intention of future use [22]. Shehadeh M *et al*, reported 49% of LOAB use [23]. Difficulty in storing due to improper packing and delivery of medication free of charge in current study settings might have contributed to the difference from previous studies. However, this practice promotes ABR by providing a source for self-medication with antibiotics without a physician's prescription [24].

Strengths and limitations of the study

The methodology used in sampling and data collection gave the study internal validity maintaining an adequate sample size, minimizing recall and reporting biases. Not highlighting the objective of the study at the initial interview was a major strength that minimized the influence on true phenomena. Conducting the study in the routine outpatient setting revealed the everyday practice and adherence levels close to real.

Due to the limited time and resources, the study was restricted to primary care settings of three categories of state-sector hospitals, and none from the private sector was included. This limits the generalizability of the study findings. Even though measures were taken to minimize the effect, the indirect over-the-phone pill counting method applied in this study had the potential to be modified by the patients thus creating social desirability bias. The study measured only the taking adherence of antibiotics but not the timing of doses which has equal importance in combating ABR.

Conclusion

Adherence to oral antibiotic prescriptions was poor among adult state sector primary care attendees in Gampaha district. Some of the sociodemographics (female gender), beliefs and practices of patients on medication, illness-related factors, therapy-related factors, and some aspects of doctor-patient communication are associated with adherence. A significant proportion of non-adherent patients had the intention to use LOAB later on.

The findings of this study have important implications for understanding the targets of future interventional strategies to improve adherence to antibiotic prescriptions in primary care attendees. As adherence significantly increases by being aware on the antibiotic prescription, primary care prescribers should be encouraged to execute their duty of making patients aware on the antibiotic prescriptions and giving

appropriate instructions clearly highlighting the importance of completing antibiotic regimens in spite of symptom improvement and repercussions of non-adherence. Alternative ways of providing information such as written information or patient education leaflets would facilitate effective patient education. Recommendation is for the primary care prescribers to consider patient's lifestyle and follow less complex antibiotic dosage schedules as far as possible. Self-medication with LOAB without physicians' advice should be discouraged by educational programmes directed to the general public. Patient educational programmes should be arranged in OPDs of hospitals using multimedia and posters in the waiting areas. All educational measures should emphasize repercussions of self-prescription with LOAB. Availability of antibiotics with simple dosage schedules at state sector primary care should be addressed at a policy level.

Future studies designed at national level including more heterogeneous population plus involvement of the private primary care, are vital. More studies measuring knowledge and attitudes towards antibiotic use would also be helpful to design appropriate educational interventions.

Author contributions

All authors made substantial contribution to conceptualize and the methodological framework of the study: acquisition, analysis and interpretation of results critically for its intellectual validity, drafting and reviewing the manuscript and final paper.

Competing interest

Authors declare nil competing interest.

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Declarations

Ethics approval

The study obtained ethical approval from the Ethics Review Committee, Post Graduate Institute of Medicine Colombo, Sri Lanka.

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