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SHORT RESEARCH REPORT

Non-adherence to antibiotic therapy in patients visiting community pharmacies

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Abstract *Background* Patient non-adherence to antibiotic therapy may lead to therapeutic failure, re-infection, and bacterial resistance. Assessing the factors associated with this problem is important for promoting rational use of antibiotics. *Objective* This study aimed to measure prevalence and reasons for non-adherence to antibiotic treatment and to identify associated factors. *Method* Patients were recruited for the study in community pharmacies in Lisbon, Portugal, from February to April, 2009. Data from prescriptions for oral antibiotics were collected for adult subjects. Adherence to treatment was assessed with a modified Portuguese version of the Morisky scale. Factors associated with non-adherence were identified through bivariate analysis and logistic regression models. *Results* A total of 243 patients were included in the study. They had a mean age 46.5 ± 16.6 years and 74.5 % of the sample was female. The prevalence of non-adherence was 57.7 % and was related to delays and failures in taking the prescribed medicine. Increasing age (OR 0.97), difficulty in buying the antibiotic (OR 2.34), duration of treatment (OR 1.28), difficulty with ingestion (OR 3.08), and satisfaction with the information given by physician (OR 0.33) were identified as independent factors associated with non-adherence. *Conclusion* Non-adherence to antibiotics is common in the community setting. Factors related to the antibiotic, the patient, and the patient-physician relationship should be addressed to promote adherence. Pharmacists should provide information to patients about correct use of antibiotics and address barriers to adherence.

Keywords Antibiotics · Bacterial resistance · Community pharmacies · Patient adherence · Portugal

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Impact of findings on practice

- There is a high prevalence of self-reported non-adherence to short-term antibiotic treatment in Portuguese community pharmacies. This raises concerns about the impact of non-adherence on the spread of bacterial resistance.
- Community pharmacists may help to improve adherence by providing patients with information about taking antibiotics as prescribed and providing strategies to avoid forgetting or delaying doses.

Introduction

Inappropriate use of antibiotics plays an important role in the spread and increase of bacterial resistance, which is a major health care issue [1, 2].

Non-adherence to antibiotic therapy is a major determinant of treatment effectiveness [3]. With regards to short-

term antibiotic treatment, non-adherence may increase the risk of therapeutic failure, re-infection and bacterial resistance which may create a subsequent need for more aggressive treatments and may lead to increased hospital admissions [4]. Determinants of non-adherence to antibiotics include factors related to medication (such as dosing regimen), to the patient (knowledge and beliefs about antibiotics), and to patient-physician relationship [5].

Portugal is one of the European countries with a higher prevalence of bacterial resistance and higher use of antimicrobials [1, 6, 7]. A Portuguese study in 2000 estimated a 40.7 % prevalence of non-adherence to antibiotics [8]. While previous studies have detailed the level of non-adherence to antibiotics, research into reasons for non-adherence to antibiotics is lacking [3, 9]. In addition to assessing the extent of non-adherence to antibiotic therapy, the present study aims to examine determinants of non-adherence to antibiotic therapy in one Portuguese city.

Aim of the study

This study aimed to measure prevalence and reasons for non-adherence to antibiotic treatment and to identify factors associated with non-adherence.

Methods

Study design and patient selection

An observational cohort study was conducted with a sample of patients using community pharmacies in Lisbon, Portugal. A sample of 100 pharmacies was randomly selected from those registered with the Portuguese National Authority of Medicines and Health Products in December 2008. The 52 pharmacies that cooperated in the study represented 62 % of the 53 Lisbon city parishes at the time. Patients eligible for the study were those aged over 18 years, who presented a prescription for one oral solid antibiotic for short-term treatment (<30 days), excluding those prescribed for prophylactic indications, and who were able to take the antibiotic by themselves and to consent to participate in the study. The study was approved by the ethics committee of the Faculty of Medicine—University of Lisbon and the Portuguese Data Protection Authority.

Data collection

After obtaining written informed consent to participate in the study, a first questionnaire was filled in the pharmacy. Pharmacists collected data about the prescribed antibiotic, including the name of the drug, the dosage, the number of units delivered to the patient, the dosing frequency, and the duration of the treatment. This information was used to estimate the conclusion date of the treatment. Patientes were contacted by telephone within 1 month of the estimated conclusion date of antibiotic therapy, for a follow-up interview. Data collected during this interview included the patients' self-report of antibiotic intake, perception and knowledge about the disease and its treatment, self-report of treatment indication, patient satisfaction with the medical consultation, regarding the information provided by the physician and patient satisfaction regarding information provided by the pharmacist. Satisfaction was measured on a three-point Likert-type scale with the following categories: very satisfied, satisfied, and dissatisfied. Patients were also asked about their difficulty in buying the antibiotic (Portuguese patients pay a defined percentage for each antibiotic and medication costs are not covered by private health insurance policies). Antibiotic drugs were classified according to Anatomical Therapeutic Chemical classification (ATC) code 3rd level [10]. Self-reported treatment indications were classified according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems [11].

Assessment of the patient adherence to antibiotic treatment

Adherence to antibiotic treatment was assessed through a modified version of the Morisky self-report scale [12], using the five questions presented in Fig. 1, with yes/no answers. Patients were classified as non-adherent if they answered 'yes' to any of the questions [13]. The last question was added to the original Morisky scale, in order to identify situations in which patients decided to take more medication than the prescribed regimen. Furthermore, patients were asked to indicate, from a pre-coded list of options, their reason for non-adherence if they either forgot to take their antibiotic or if their dosage timings differed from those in the prescribed dosing schedule.

In a secondary analysis, the modified adherence scale was adjusted for compliance with timing of antibiotic intake. In this adjustment, the 'yes' answers to question 2 were classified as non-adherence situations only if the patient also reported a delay regarding the intake schedule greater than 2 h for once daily antibiotic regimens, or greater than 1 h for the remaining regimens [14]. This approach assumes that patients reporting longer delays in the expected intake schedule will be at higher risk of antibiotic failure [15].

Statistical analysis

The sample size calculation assumed a prevalence of non-adherence of 30 % within ± 10 % of the true value, and

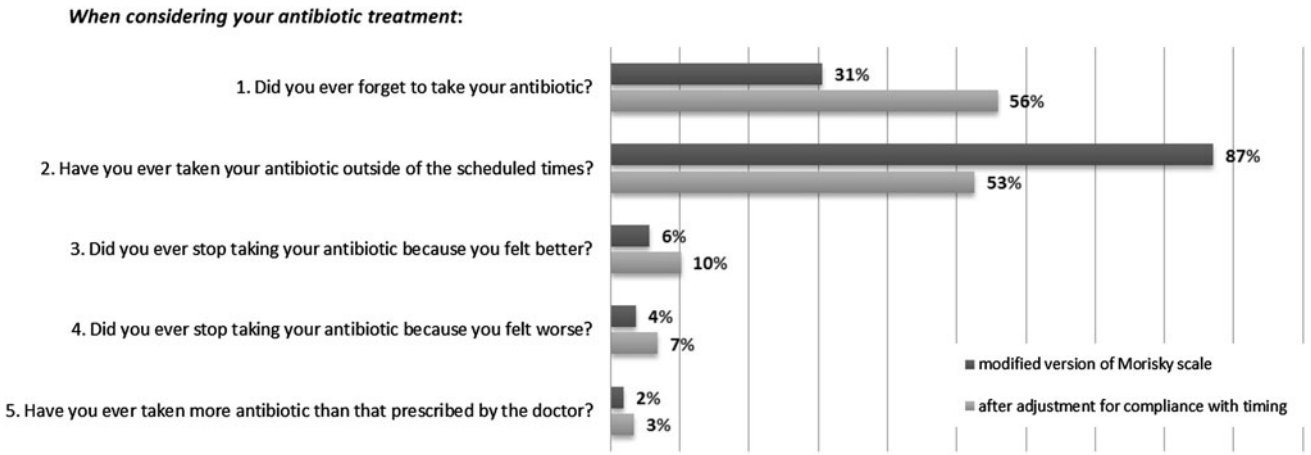

Fig. 1 Prevalence of non-adherence behaviours, according to the self-reported non-adherence scale after adjustment for compliance with timing. Since a non-adherent patient could present more than one behaviour, the sum of relative percentages does not equal 100 %

significance set at $\alpha = 0.05$. After a descriptive analysis of the sample characteristics, the Mann–Whitney and χ^2 test (or Fisher's exact test) were used for a bivariate analysis of non-adherence for numeric or categorical variables, respectively ($\alpha = 0.05$). A multivariate analysis was also conducted. Variables with a likelihood-ratio test with a $P < 0.25$ were entered in a stepwise logistic regression (backward step with decision based on minimum Akaike Information Criteria). Odds ratios (OR) and 95 % confidence intervals (95 % CI) were estimated for the final model. All statistical analyses were performed on the R project for statistical computing (http://www.r-project.org), an open-source software environment for statistical computing and graphics [16].

Results

A total of 339 patients were recruited at the pharmacies from February to April 2009. Twenty seven (8.0 %) of these patients refused to participate due to lack of interest (44.4 %), lack of time (22.2 %) or other reasons (14.8 %) with 18.5 % reporting no reason for their refusal to participate. Of the remaining 312 patients, it was not possible to contact 46 (14.7 %) and 16 (5.1 %) refused to answer the questionnaire. Seven participants were excluded since they stopped antibiotic treatment at their physician's request. Hence, 243 (77.9 %) participants were included in the study sample. The mean age was 46.5 ± 16.6 (mean ± standard deviation) years, 74.9 % of the participants were female and 59.9 % had secondary school or higher educational level.

Regarding the antibiotic prescription, patients received penicillins (49.4 %), macrolides (23.5 %) quinolones (16.4 %), and other (10.7 %) antibiotics. The self-reported reasons for treatment were diseases of the respiratory system (46.8 %), digestive system (25.8 %), genitourinary tract (15.0 %), skin and subcutaneous tissue (4.7 %), ear (3.9 %), and other (3.8 %). The majority of participants were satisfied or very satisfied with the information given by their physicians (54.8 and 31.7 %, respectively). Of the participants that received information at pharmacy (58.1 %), all were satisfied or very satisfied with the information given (50.4 and 49.6 %, respectively).

Prevalence and reasons for non-adherence

Of the 243 initial participants, 0.8 % (n = 2) did not start the treatment, due to "feeling better meanwhile" or "having no problems again". Of the remaining 241 participants, 44.8 % (n = 108, 95 % CI 38.4–51.3 %) were non-adherent according to the modified version of the Morisky scale (Fig. 1). From the 33 patients who had forgotten to take the antibiotic, 45.5 % did not state any specific reason ("simply forgot"), 18.2 % reported "having left the antibiotic at home", 15.1 % "were busy", 9.1 % "were sleeping" and 12.1 % provided other reasons. Amongst the 94 respondents who failed to adhere to the timings of their dosage schedule, 46.8 % "simply forgot to take it on time", 17.0 % were "doing something else (working/studying/…)", 11.7 % reported "having left the antibiotic at home", 11.7 % "were sleeping", 5.3 % reported other reasons and 7.4 % did not answer. The median (interquartile range) delay for ingestion was 60 (30–120) min. In the secondary analysis, non-adherence prevalence diminished to 24.5 % (n = 59, 95 % CI 19.3–30.5 %) when considering the adjustment for compliance with timing (Fig. 1). From the 108 non-adherent patients, 96.3 % answered 'yes' to one or two questions of the modified version of the Morisky scale (75 and 21.3 %,

Table 1 Factors associated with self-reported non-adherence

Variables	Adherent patients (n = 103)	Non-adherent patients (n = 85)	OR	95 % CI
Age (years), mean (standard deviation)	48.2 (17.1)	42.3 (15.0)	0.97	0.95–0.99
Duration of treatment (days), median (IQR)	8.0 (5.0–8.0)	8.0 (8.0–8.0)	1.28	1.11–1.46
Difficulty in buying the antibiotic, n (%)				
None	86 (83.5)	62 (72.9)	Reference	
Any	17 (16.5)	23 (27.1)	2.34	1.06–5.14
Difficulty with taking the antibiotic, n (%)				
None	92 (89.3)	64 (75.3)	Reference	
Any	11 (10.7)	21 (24.7)	3.07	1.31–7.23
Satisfaction with the information given by physician, n (%)				
Unsatisfied	8 (7.8)	15 (17.6)	Reference	
Satisfied/very satisfied	95 (92.2)	70 (82.4)	0.33	0.12–0.92

The model is considered adequate by the Hosmer–Lemeshow test ($p = 0.31$). ROC curve estimates: area under the curve 0.762

IQR, interquartile range; OR, multivariate adjusted odds ratio estimates; 95 % CI, confidence interval with $\alpha = 0.05$ for the presented OR estimates

respectively) and 3.7 % answered 'yes' to three or more questions.

Factors associated with non-adherence

The bivariate analysis identified several variables as being significantly associated with non-adherence (modified version of the Morisky scale). Increasing age ($p = 0.03$) and single daily dose ($p < 0.001$) were associated with lower risk of non-adherence. Difficulty with buying the antibiotic ($p = 0.05$), difficulty with taking the antibiotic ($p = 0.03$), increasing duration of treatment ($p < 0.001$) and increasing time between the prescription and the antibiotic purchase ($p = 0.04$) were associated with higher risk of non-adherence. Marital status was associated with non-adherence ($p = 0.01$), with a higher proportion of non-adherent patients among those who were single than in those who were married. An association was also found with ATC code 3rd level ($p = 0.01$), with more non-adherent patients among those that received quinolones (J01M) and other antibiotics (J01A tetracyclines, J01E sulfonamides and trimethoprim and J01X other antibacterials) than penicillins (J01C), other beta-lactam antibacterials (J01D) or macrolides (J01F). Regarding other variables, no association was found with having read the package leaflet or receiving information regarding the antibiotic at the pharmacy.

From the final logistic regression model, with complete data from 188 participants (Table 1), increasing age, difficulty in buying the antibiotic, duration of treatment, difficulty with taking the antibiotic, and satisfaction with the information given by physician were identified as independent factors associated with non-adherence.

Discussion

The present study estimates that nearly 45 % of the patients in this sample were non-adherent with antibiotic treatment. This result is similar to the one obtained in the Portuguese study in 2000, but higher than the figure of 22.3 % found in an international study conducted in 2005 [4, 8]. This may be due to different definitions and measures of non-adherence and different sampling strategies. After adjusting for compliance with timing, the prevalence of non-adherence was 31.5 %. Although this adjustment seems to be relevant from the pharmacokinetic point of view [14, 15], it is also recognized that patient self-report may be prone to social desirability bias, regarding questions about timing. It would be interesting to assess differences in clinical outcomes related to the two measurement approaches in future studies.

A threefold increase in the risk of non-adherence was observed when patients reported difficulty with taking the antibiotic. This was also described in other studies [3] and emphasizes the need to improve the formulation of antibiotics to improve adherence.

The duration of antibiotic treatment also increased the risk of non-adherence. Each additional day of treatment resulted in an increase of 28 % in the odds of non-adherence. Similar findings have been reported in other studies [3].

Patient-related variables were also associated with non-adherence. Increasing age was associated with a decreased risk of non-adherence, in accordance with other studies regarding short-term antibiotic therapy [4] and several chronic conditions [17, 18]. Self-reported difficulty in buying the antibiotic also increased the risk of non-

adherence to antibiotic treatment [4]. Physicians and pharmacists should consider simple regimens and less expensive options when prescribing and dispensing to prevent non-adherence. Satisfaction with the information given by the physician (regarding the antibiotic) diminishes the odds of non-adherence by 67 %. This observation is in line with the results from other multi-national studies [4].

Only 58 % of the participants reported having received information regarding the antibiotic at the pharmacy. This figure is lower than the one reported in a 2006 Swedish study, where 74 % of the overall population stated that pharmacy personnel often provide information on antibiotic use [9]. Although no differences in non-adherence were found when considering patient satisfaction with the information provided at pharmacy, other studies (regarding several chronic diseases) suggest that pharmacists should reinforce and clarify physicians' instructions regarding treatment and ascertain probable barriers to non-adherence [19, 20].

Study limitations

Self-reported non-adherence may be affected by social desirability bias [4]. Hence, the real prevalence of non-adherence may be higher than that observed in this study. The modified version of the Morisky scale was previously validated [12] and the included questions provided information regarding reasons and behaviours of non-adherence to antibiotic treatment. Another limitation is that the study sample might not be representative of the overall population, since it includes mainly females and participants with a higher educational level. A representative national sample would be advisable to confirm the prevalence of non-adherence and to explore other questions, such as awareness of proper antibiotic use and the relation between non-adherence and resistance [9].

Conclusion

Non-adherence to antibiotic treatment seems to be frequent among patients using community pharmacies. It appears to be mainly due to forgetfulness or delays in taking antibiotic doses. Factors related to the antibiotic regimen (duration of treatment, formulation characteristics), to the patient (younger age, difficulty in buying the antibiotic) and to the patient-physician relationship (satisfaction with the information given by physician) should be addressed when promoting adherence to antibiotic treatment. Community pharmacists may help patients to avoid forgetting or delaying doses by emphasizing that the benefits of taking antibiotics outweigh the risks associated with their use, and by providing patients with reminder strategies.

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Conflicts of interest None to declare.

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