Pattern of antibiotic use in the community: Non-adherence and self-prescription rates in an Italian urban population

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Abstract. The aim of the present study was to assess the pattern of antibiotic use in a community setting of an urban area of Italy and identify factors that affect adherence to their use. By using a questionnaire-based survey, we collected 1,269 interviews and performed analysis on those patients who had their last course of antibiotic within the past 12 months (956 subjects). Among the subjects reporting that they had not followed their last antibiotic course as prescribed, 14.7% stopped therapy early, 5.4% modified the dosage, and 5% changed the prescribed antibiotic. Approximately 23% of the subjects declared that they self-prescribed antibiotics. After adjusting for all covariates, major predictors for the self-prescription of antibiotics were younger age, female gender and higher socioeconomic and educational status. Conversely, both low educational and socioeconomic status were associated with a higher risk of non-adherence to physician indications. The findings of this study assessed the widespread pattern of poor antibiotic-taking behavior and provides important implications for understanding the targets of future educational campaigns to control the use and misuse of antibiotics.

Introduction

Non-adherence is defined as the extent to which an individual's behavior (taking medication, following a diet and/or executing lifestyle changes) corresponds with the agreed recommendations of a healthcare provider (1). Specifically, non-adherence to medication is defined as the attitude of a patient for not taking a prescribed medication or following a prescribed course of therapy. Although non-adherence to medication is often related to chronic conditions, a significant percentage of patients are not fully compliant with basic medication for acute diseases, including antibiotics. Antibiotics are among the most commonly used medicines worldwide. Italy has the third highest number of antibiotic prescriptions in Europe (2). Data collected by the National Observatory on the Use of Medicines (Osservatorio Nazionale Sull'impiego dei Medicinali, OsMED) reported that in Italy the cost of antibiotics amounts to 1,204 million euros in the community setting and 1,265 million euros in public healthcare structures. Antibiotics account for the fourth leading medicine in terms of expenditures and ninth for prescribed quantities. They are mostly prescribed in the marginal range of age – less than 4 years and more than 65 years – but in recent years there has been a progressive increasing usage in subjects between 15 and 64 years of age. Finally, throughout the country, there is a high regional variability in the number of antibiotic prescriptions and a consistent geographic trend with a deviation from the national average by more than 20% in the southern regions and islands (3). Despite their importance, improper use of antibiotics contributes to the emergence of antimicrobial resistance. In fact, the phenomenon of resistance has been attributed both to indiscriminate overuse and misuse of antibiotics (4,5). At present, antibiotic resistance is one of the major public health threats worldwide leading to antimicrobial drug-resistant strains and making bacterial infections more difficult to treat (6-10).

Poor adherence to antibiotic regimens has resulted in one of the major causes of treatment failure. Non-adherence to antibiotic treatment has been widely demonstrated to have a profound negative impact on patient health resulting in the reduction of clinical success (11), additional physician visits, extra drug prescriptions and hospital admissions with an increase in additional costs to manage non-adherent patients (12). Intervention to reduce antibiotic misuse must include both patient and physician education concerning the appropriate use of antibiotics. Nevertheless, before starting an intervention program, public health workers need to know the impact of the phenomenon in the community setting in which the intervention should be addressed, and to identify the characteristics of the population related to the attitude of non-adherence.

The present study was aimed at deepening our knowledge of patient non-adherence with antibiotic treatment in an Italian urban setting and identifying patient characteristics that predict a worse compliance. Specifically, the study focused on self-prescription and the use of recycled antibiotics as well as determining which subjects in our community do not follow antibiotic regimens as prescribed. We also evaluated factors associated with such antibiotic abuse and misuse. By iden-

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tifying the target population, more appropriate educational support can be implemented and more effective interventions aimed at improving patient compliance may be designed.

Subjects and methods

Study population. The study survey was carried out in Catania (approximately 300,000 inhabitants), a city on the east side of Sicily, Italy, from October 2009 through October 2010. Information was recorded from structured, closed-question data forms. The population included in the study was selected by a randomized sampling of 13 outpatient clinics with general practitioners. All clinics were located in urban areas, serving a total population of approximately 19,000 patients. Each district of the city was involved in distributing the questionnaires to at least one outpatient clinic depending on the number of inhabitants of the served zone.

Data collection. Questionnaires were developed to collect information related to demographics and the most recent use of antibiotics within the last year. Demographic data in the first part of the questionnaire included age, gender, level of education and occupation. With regard to employment status, we used codes supplied by the Office for National Statistics (ONS) to characterize the professional status of the subjects in 4 groups as shown below: i) unemployed and housewives, ii) unskilled occupations, iii) partly skilled and skilled occupations, and iv) professional and managerial occupations. Educational level included 3 groups according to the highest level of education attained by the subject: i) none, elementary or secondary school, ii) high or technical school, and iii) university.

The second part of the questionnaire posed questions concerning the cause leading to the most recent antibiotic intake within the past 12 months. Only the data of respondents that used antibiotics within the last year were considered eligible for analysis. Participants were asked questions concerning the relative adherence with their last treatment course (i.e. Did you take the required number of daily doses over the full duration of the course? Did you modified the dosage? Did you change the antibiotic?) as well as questions aimed to assess the use of self-prescribed antibiotics without the advice of a physician (i.e. Did you take antibiotics without a prescription? Did you follow the advice of your doctor?). The questionnaires were anonymous and verbal consent was obtained from all the subjects before compiling the data.

Outcome measures. We used the term 'adherence' to refer to the degree of conformity with the indications of the physician (length of the treatment course, number of doses, and type of antibiotic) and the term 'self-prescribe' to refer to the behavior of a patient to use antibiotics without advice from the doctor. We analyzed the demographic characteristics affecting non-adherence with prescribed antibiotics or self-prescription to identify potential predictors of poor compliance. We defined 'non-compliant' as a subject who self-prescribed antibiotics and/or who did not adhere to the physician's prescription.

Statistical analysis. Categorical data were presented as frequency of occurrence. The Chi-square test for categorical data was used to examine bivariate relationships between self-prescribing and non-adherence according to demographic characteristics. A stepwise logistic regression model was computed for the dependent variables of self-prescription and non-adherence to the antibiotic course with the same set of variables to determine the best predictors of these behaviors. Multivariate regression was used to calculate the odds ratios (ORs) for the trend to self-prescribe antibiotics and not adhere to physician indications where 95% confidence intervals (CIs) were based on the estimated standard errors. All tests were two-tailed with α levels of 0.05 considered significant.

Data were entered into Microsoft Excel for Windows (Microsoft Corporation, Redmond, WA, USA). Statistical analysis was performed using SPSS for Windows release 17.0 (SPSS Inc., Chicago, IL, USA).

Table I. Demographics and pattern of antibiotic use of the study population (n=956).

	Respondents	
	%	n
Antibiotic use within the last year		
Respiratory tract infections	59.7	571
Gastrointestinal tract infections	16.2	155
Infections at other sites	24.1	230
Age		
<25 years	10.1	97
25-44 years	24.0	229
45-65 years	36.3	347
>65 years	29.6	283
Gender		
Male	43.1	412
Female	56.9	544
Level of education		
Elementary or secondary	52.5	502
High school	28.9	276
University	18.6	178
Occupation		
Unemployed	20.2	193
Unskilled occupations	15.4	147
Partly skilled occupations	48.4	463
Skilled occupations	16.0	153
Non-compliant patients	45.0	430
Self-prescribed antibiotics	22.7	217)
Did not consult the physician	37.0	80
Non-adherence to physician indications	25.8	247
Did not complete the course	14.7	139
Modified the drug dosage	5.4	51
Changed the drug	5.0	47

Results

Eleven of the 13 general practitioners agreed to participate in the study resulting in a total of 1,269 subjects completing the

Table II. Self-prescription and non-adherence to antibiotic use with respect to the study variables.

	Self-prescription			Non-adherence to prescription		
	No (n=716) % (n)	Yes (n=217) % (n)	P-value	No (n=709) % (n)	Yes (n=247) % (n)	P-value
Age, % (n)			<0.001			0.226
<25 years	10.9 (78)	8.3 (18)		9.2 (65)	13.0 (32)	
25-44 years	19.7 (141)	39.6 (86)		23.4 (166)	25.5 (63)	
45-65 years	35.1 (251)	38.7 (84)		37.7 (267)	32.4 (80)	
>65 years	34.3 (246)	13.4 (29)		29.8 (211)	29.1 (72)	
Gender, % (n)			<0.001			0.947
Male	46.6 (334)	31.8 (69)		43.2 (306)	42.9 (106)	
Female	53.4 (382)	68.2 (148)		56.8 (403)	57.1 (141)	
Level of education, % (n)			<0.001			<0.001
Elementary or secondary	56.8 (407)	37.8 (82)		47.0 (333)	68.4 (169)	
High school	28.9 (207)	28.1 (61)		32.6 (231)	18.2 (45)	
University	14.3 (102)	34.1 (74)		20.5 (145)	13.4 (33)	
Occupation, % (n)			<0.001			<0.001
Unemployed	22.1 (158)	12.9 (28)		18.3 (130)	25.5 (63)	
Unskilled occupations	17.6 (126)	9.7 (21)		11.8 (84)	25.5 (63)	
Partly skilled occupations	47.1 (337)	51.6 (112)		51.8 (367)	38.9 (96)	
Skilled occupations	13.3 (95)	25.8 (56)		18.1 (128)	10.1 (25)	

questionnaire. Nine hundred and fifty-six respondents (~75%) reported that they had been prescribed an antibiotic within the last year. The demographic characteristics of the subjects that reported antibiotic use during the last year and their patterns of use are shown in Table I. Those respondents which were prescribed an antibiotic in the last year were women, older than 45 years and with a lower level of education. The majority of the respondents completed the course (~85%). Among those reporting that they did not follow their last antibiotic course as prescribed, 14.7% stopped therapy early, 5.4% modified the dosage, and 5% changed the prescribed antibiotic. Moreover, approximately 23% of the subjects declared self-prescription of antibiotics and 37% of them did not consult a physician after using them. Thus, a total of 45% of patients were non-compliant with antibiotic therapy.

Characteristics of the study population in respect to their non-compliant attitude (namely self-prescription and non-adherence with physician indications) are presented in Table II. Respondents more likely to self-prescribe antibiotics were middle class female with a higher educational level and occupational status (P<0.001). On the other hand, subjects who did not adhere to physician indications were found to have a lower level of education and occupational status (P<0.001). No statistically significant relation was found for gender and age.

The multivariate logistic regression model is shown in Table III. After adjusting for all covariates, the major predictors for self-prescription of antibiotics were younger age, female gender and higher educational level and occupational status. Specifically, a higher risk for the self-prescription of antibiotics was found for patients 25-44 years of age (HR, 5.01; 95% CI, 3.06-8.19; P<0.001), while subjects with an elementary school education and those with unskilled occupations had a lower risk (HR, 0.39; 95% CI, 0.26-0.61; P<0.001 and HR, 0.35; 95% CI, 0.19-0.65; P=0.001, respectively).

With regards to adherence to physician indications, the multivariate logistic regression model revealed that both low educational level and occupational status were associated with a higher risk of non-adherence. In detail, patients who completed elementary school had a higher risk than those who achieved a university degree (HR, 1.77; 95% CI, 1.13-2.75; P=0.012) as well as unemployed and subjects with unskilled occupations (HR, 1.82; 95% CI, 1.04-3.13; P=0.035 and HR, 2.82; 95% CI, 1.61-4.94; P<0.001, respectively).

Discussion

This study evaluated variables associated with poor compliance with antibiotics therapy. Results indicated that multiple factors are related to the non-compliance of individuals. Specifically, differences in patient characteristics were found to distinguish between those who did not follow the therapy as prescribed (stopping early, modifying the dosage, or changing the drug) and those who self-prescribed antibiotics.

The study revealed that nearly a quarter of the subjects use non-prescribed antibiotics in the Sicilian urban population. Moreover, a relatively high percentage of respondents discontinued therapy early and admitted to not following the recommended dosage or even to substituting the antibiotic. Several of the most recent reviews reported similar rates compared to our results, revealing that compliance was generally unsatisfactory (13-15). Although there is a substantial heterogeneity in the definition of 'non-compliance', the

Table III. Significant predictors from stepwise logistic regression for self-prescription and non-adherence to antibiotics.

	Self-prescription		Non-adherence with prescription	
Variables	OR (95% CI)	P-value	OR (95% CI)	P-value
Age			NS	-
<25 years	2.25 (1.15-4.42)	0.019		
25-44 years	5.01 (3.06-8.19)	<0.001		
45-65 years	2.72 (1.69-4.39)	<0.001		
>65 years	1	-		
Gender			NS	-
Male	0.54 (0.38-0.76)	<0.001		
Female	1	-		
Level of education				
Elementary or secondary	0.39 (0.26-0.61)	<0.001	1.77 (1.13-2.75)	0.012
High school	0.41 (0.26-0.64)	<0.001	0.79 (0.48-1.31)	0.359
University	1	-	1	-
Occupation				
Unemployed	0.37 (0.21-0.65)	0.001	1.81 (1.04-3.13)	0.035
Unskilled occupations	0.35 (0.19-0.65)	0.001	2.82 (1.61-4.94)	<0.001
Partly skilled occupations	0.66 (0.43-1.02)	0.062	1.11 (0.67-1.81)	0.693
Skilled occupations	1	-	1	-

results from the large number of studies appear to agree on these rates. However, one of the major challenges regarding this issue remains differences in the measurement methods of non-compliance. In fact, the distinction between predictors of misuse and those of abuse was poorly differentiated, identifying such unhealthy behaviors under the general terms of non-compliance or non-adherence. Yet, collectively, these estimates of compliance showed a widespread pattern of poor antibiotic-taking behavior.

Notably, we found in our population that the subjects who were more likely to abuse antibiotics without consulting a physician and, in contrast, those who were more prone not to follow the drug protocol as prescribed, had opposing characteristics. In fact, individuals with a lower educational level and occupational status tended to misuse antibiotics while those with a higher level tended to abuse drugs. Other studies revealed similar (16) or lower rates (17), but equal predictive factors of self-medicated drug use. One could speculate that the attitude of the patient may reflect the level of knowledge concerning antibiotics. In fact, greater knowledge concerning antibiotics was associated with a greater tendency to keep leftover antibiotics and use them without advice from a clinician. Medical awareness of patients with a high socioeconomic and educational status may play a role in the increased use of non-prescribed antibiotics. Thus, subjects with a higher level of education and a higher socioeconomic status may be more likely to feel confident in diagnosing an illness and, consequently, in self-prescribing an antibiotic therapy. However, the fact that part of such a population consists of doctors should be considered as a possible source of bias since self-prescribing behavior rates may be strongly influenced by their presence.

Conflicting observations have been shown regarding the role of age in non-adherence to antibiotic therapy. Several studies reported that patient age has no impact on adherence (18), while other studies found higher rates of non-adherence of antibiotics in younger (15) and in older patients (19). In the present study, younger subjects were more prone to be less compliant. In fact, in accordance with a global survey, there was a negative correlation between patient age and both self-prescription and non-adherence to the prescription of their physician (15). This may depend on the relationship between the patient and the general practitioner. In fact, younger patients are more likely to be non-compliant as they perceive greater freedom than older patients with regard to the use of drugs and the advice of physicians.

With regard to gender, experts do not agree on the true role of gender in determining attitudes of non-compliance (13). However, our study showed that female gender was a predictive factor of a non-compliant attitude even if this result was due to a greater number of women taking antibiotics in our study population.

Antibiotics are widely used both in the community and in the hospital setting. Nevertheless, their effectiveness is strongly related to how such medications are used by the patients, particularly in the community setting. Previous studies reported that patients admit to discontinuing antibiotic therapy when they begin to feel better or due to the onset of adverse events (20,21). The use of recycled medications and the phenomenon of self-prescribing antibiotics are the severe consequences of poor compliance with antibiotic therapy. In our study, we found higher rates for self-prescription than in poor adherence with prescribed antibiotics. Although leftover antibiotics result from a discontinuation of prior treatment,

it may also be influenced by the packaging and medication dispensing of the drug. In fact, in countries such as Italy, where drugs require pre-packaged doses of medication, a greater quantity of medication is dispensed than is required, resulting in the availability of leftover doses even after completion of the prescribed regimen (22). Antibiotic resistance is mainly attributed to the indiscriminate overuse of antibiotics yet doctors may also play a role in this issue. Several investigators have reported inappropriate prescribing practices by physicians in the outpatient setting. Indeed, most of the studies revealed that about half of patients with a common cold are often treated with antibiotics (23,24), instead of a more discriminate use (25). The reasons why physicians inappropriately prescribe antibiotics for conditions that can be cured without using such a therapy can be explained by patient expectations (26). In fact, clinicians report that they often prescribe antibiotics since they perceive that patients want them (27). Patient beliefs concerning the expectations for and effectiveness of antibiotics for minor illnesses play a key role in the unnecessary use of antibiotics (28). Although patient expectation and perceived antibiotic efficacy depend on several factors such as the length of treatment course, time to the onset of symptom relief and time to complete resolution of symptoms (29), their attitude about the need for antibiotics often depends on the behavior of their physician. It is not surprising that in a study conducted in the outpatient setting, patients whose doctors routinely prescribed antibiotics for cold symptoms were more prone to use antibiotics without the advice of a physician (30). Finally, diagnostic uncertainty may also be addressed as a cause of inappropriate prescription (31).

The findings in this study have important implications for understanding the targets of future educational campaigns to control the use and the misuse of antibiotics. Results addressed a need for culturally tailored interventions to more effectively educate the population. Interventions to improve adherence designed by public health workers should include counselling on the importance of adherence as well as educational campaigns appropriately tailored to the target population according to the findings assessed in this study. Furthermore, some campaign strategies may include the distribution of educational materials (posters, brochures) educating the population to the correct use of antibiotics, (32) suggesting over-the-counter remedies (33) and relief strategies for viral infections as better therapies (34). In combination with these public health interventions, general practitioners should minimize antibiotic misuse by reducing regimen complexity, including lower dosage frequency and shorter therapy durations (35). Moreover, the use of written instructions and reminder devices to improve adherence and compliance with antibiotic therapy should be implemented and clearly stated. Finally, physician education should be aimed at providing more extensive knowledge to improve the quality of antibiotic selection (36).

This study has some limitations that warrant discussion. First, one limitation may depend on the methodology used to assess non-compliance. In fact, data concerning antibiotic misuse was reliant on patient self-reporting and so the level of non-compliance is likely to be an underestimate of the true phenomenon. However, the objective of the study was not only to estimate the absolute figures of the community, but rather to examine factors that may be associated with patient non-adherence to antibiotic regimens and suggest ways in which these issues can be addressed. Moreover, there are currently no standardized, validated instruments with which to measure adherence to antibiotic therapy and patient-reported adherence is one of the most frequently used methods to obtain subjective estimates.

Another limitation is that patients were asked several questions about their past use of antibiotics which may have led to recall bias. Moreover, given the cross-sectional nature of the study and the use of a questionnaire to further define the scope of patient antibiotic misuse, the possibility that respondents may have misunderstood or misinterpreted questions should be taken in account. In fact patient may not be able to identify whether a medication is an antibiotic or not, contributing to the creation of biases. However, this study had various strengths. The population size was sufficiently representative of the urban setting of the city. Moreover, this study is the only study conducted in Sicily and, also, one of the few in the whole Italian setting. Thus, we consider the recognition of such issues in our country crucial due to the current policy of medication packing that inevitably contributes to the self-prescription of drugs.

Future studies designed on a large-scale and aimed at including a more heterogeneous population mix to be more representative of the whole Italian population are needed. More studies measuring the knowledge and attitudes toward self-prescription practices would also be helpful to design appropriate interventions. Antibiotic use in the community must be improved through targeted intervention aimed at increasing the education of patients and physicians on the appropriate use of antibiotics. Topics dealing with the dangers of using recycled antibiotics and, on the other hand, adherence to physician prescriptions should be addressed to individuals of a higher and lower education level, respectively. However, a general message towards the community aimed at improve compliance with antibiotics is needed. Moreover, the high cost of non-compliance on healthcare expenditure as well as the benefits on patient health, warrant using such interventions.

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