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Antibiotherapy management of respiratory infections in ambulatory in Tunisia

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Abstract

Ear, Nose & Throat (ENT) and acute respiratory tract (ART) infections are the main causes of inappropriate antibiotic prescribing. To evaluate the antibiotics prescribing practices for these infections, we conduct an observational study with 23 general practionners (GPs) working in private offices of the East Central Region of Tunisia.

Among the 374 patients presenting ENT or ART infections, 193 were men (51.6%). The mean age was 45.6 ± 16.7 years. Comorbidities were present in 174 patients (51.9%). The first visit was made 3.7 ± 6 days after the beginning of the symptoms. The main diagnoses are acute bronchitis (37.4%), tonsillitis (33.4%) and acute maxillary sinusitis (20.9%). Additional tests (chest-X-ray and Lab-test) were prescribed for only 75 patients (20%). An antibiotic was prescribed for 360 patients (96.2%), for an average of 9.1 ± 2.3 days. The main prescribed antibiotics are β-lactams (58.3%), fluoroquinolones (23.5%) and macrolides (15.6%). Overall, the rate of inappropriate antibiotic prescription was 34.1%, the highest rates was noted in Exacerbation of the COPD (73.2%) and pneumonia (42.1%). Antipyretics and corticosteroids were prescribed in 71.4% and 44.7% respectively. The clinical success rate was noted in 375 cases (89%). The average cost of an infectious episode amounts to about $ 45 ± 20.

This study underlines over-prescribing of antibiotics with unnecessary additional costs which may be related to the non-use of diagnostic tools. National guidelines should be developed in order to reduce unnecessary antibiotic prescription and emerging of bacterial resistance.

Keywords

ENT Infections; Respiratory Tract Infections; Antibiotic Prescription; Bacterial Resistance.

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Introduction

Acute respiratory tract infections are the commonest acute conditions managed in general practice. They are also the main causes of antibiotic prescribing. These antibiotic prescriptions are often inappropriate or unnecessary and may contribute to the development of resistance among the causative bacterial agents of community infection [1-4]. In Tunisia, the rates of antibiotic prescriptions remain high in general practice [5, 6].

The high rate of antibiotic prescription may be explained by the absence of national recommendations, the lack of diagnostic tools that can help to guide the prescription, probably pressure from patients and the absence of education actions to promote the appropriate use of antibiotics.

The antibiotic prescribing practices of general practitioners (GPs) has been rarely studied in Tunisia. Knowing the attitude of peers, when facing an Ear-Nose-Throat (ENT) and respiratory tract infection, can encourage them to change their habits.

The AMIRAT (Antibiotherapy Management In Respiratory Infections in Ambulatory in Tunisia) study aims to evaluate the prescribing practices of general practitioners when facing an ENT or a respiratory infection in Tunisia and their direct cost.

Patients & Methods

This observational study on the use of antibiotics in ENT and respiratory infections, was conducted from February 1st, 2014 (date of the first inclusion) to November 25th, 2014 with 23 GPs (General practitioners) working in private offices of the East Central Region of Tunisia (Governorates of Sousse, Monastir and Kairouan) and who have agreed to conduct the study.

The study was approved by ethic committee of the Teaching Hospital of Monastir and conducted in accordance with Good Clinical Practice [7] and the Declaration of Helsinki [8]. Written informed consent was obtained from all participants prior to study commencement.

The inclusion criteria was men or women aged 18 years or more with a clinical symptoms of an upper or lower respiratory tract infection and possibility of a clinical monitoring.

Patients who do not meet the inclusion criteria, pregnant women and patients who require hospitalization were excluded.

The clinical monitoring includes two visits, the inclusion visit (V1) and the visit after 8 ± 3 days (V2).

The GPs were free to decide which laboratory or radiological tests may be performed and which antibiotics, monotherapy or combination, should be prescribed. The diagnosis was based on definitions of ENT and respiratory tract infections (pharyngitis, acute otitis media, acute maxillary sinusitis, acute bronchitis, pneumonia, acute exacerbation of chronic obstructive pulmonary disease-COPD) [9] and provided to prescribers with the case report form (CRF).

The primary objective was to evaluate antibiotic prescription (drug, dosage regimen and duration) related to the clinical diagnosis.

The secondary objective was to estimate the global cost of clinical entity.

The diagnosis were analysed by age. In the evaluation of prescription, the antibiotic prescription was considered as inappropriate when the antibiotic spectrum of activity does not include the bacteria usually responsible for the infection or the antibiotic is unnecessary for the responsible bacteria or when the dose and duration of the antibiotic are insufficient. The clinical success of treatment was evaluated by the treating physician.

The calculation of costs was based on the public prices of drugs, according to the nomenclature of the National Health Insurance Fund (NHIF) for the year of the study and according to the amount spent for additional tests. The NHIF estimates the cost of a consultation was 18 Tunisian dinars (TND).

Data were entered on the Epi Data, and analysed using the STATA© software.

A statistical analysis was carried out, p-value less than 5% was considered as statistically significant.

Results

The study involved 374 patients, among them 193 men (51.6%) and 181 women (48.4%). The mean age was 45.6 ± 16.7 years. More than three quarters of the patients (77.5%) live in urban areas, 86.4% were schooled, 91.7% had a satisfactory socioeconomic level and 72% were affiliated with the NHIF.

Comorbidities were noted in 174 patients (51.9%). The commonest comorbidities were hypertension (15.2%), chronic respiratory disease (13.4%) and diabetes (9.9%). Seven patients (1.9%) had a beta-lactam's hypersensitivity. Body mass index (BMI) showed overweight (BMI: 25 to 29.9 kg/m^2) in 142 patients (38%) and obesity (BMI ≥ 30 kg/m^2) in 69 patients (20%).

The first visit was made after 3.7 ± 6 days (median: 2 days) after the beginning of the symptoms.

The main clinical diagnoses are shown in **Table 1**. Only one diagnosis was retained in 330 patients (88.2%) and two or more diagnoses in 44 cases (11.8%). The most frequent diagnostic combinations were tonsillitis with acute bronchitis (10 cases) and acute otitis media with acute bronchitis (10 cases).

Table 1. The main clinical diagnosis of patients.

Domains/Facets	Number	%
One main disease	330	88.2
Acute bronchitis	116	31.0
Tonsillitis	99	26.5
Acute maxillary sinusitis	57	15.2
Exacerbations of COPDs	28	7.5
Pneumonia	16	4.3
Acute otitis media	12	3.2
Others	2	0.5
More than one disease	44	11.8
Total	374	100.0

The analysis of investigated patients according to age shows that tonsillitis was significantly more prevalent among young patients, and the frequency decrease significantly with age, from 48.3% in patients between 18 to 29 years to 12% in patients aged 60 years and older (p< 0.001). It was the same for acute maxillary sinusitis with 28.8% to 13.3%, respectively (p=0.002).

In contrast, the frequency of acute bronchitis, pneumonia and chronic obstructive pulmonary disease (COPD) exacerbations increased significantly with age, from patients aged 18-29 years to patients older than 60 years, 1.1% to 8% (p=0.009), 22.5% to 46,7% (p=0.04) and 0% to 28% (p<0.001) respectively.

Additional tests were prescribed for 75 patients (20%). The main additional requested tests were chest X-ray (n=54, 14.4%), C-reactive protein (n=24, 6.4%), fasting plasma glucose (n=22, 5.9%) and complete blood count (n=22, 5.9%).

An antibiotic was prescribed for 360 patients (96.2%), 347 patients received only one antibiotic and 13 (3.5%) received two or more. The main prescribed antibiotics are shown in **Table 2**.

Table 2. The main prescribed antibiotics.

Antibiotics			Frequencies %
β-lactams			
Penicillins	Amoxicillin-clavulanic acid	41.8	71.5
	Amoxicillin		26.5
	Penicillin V		2.0
Cephalosporins	Cefuroxime (2nd GC)	16.5	65.6
	Cefpodoxime (3th GC)		31.1
	Cefixime (3th GC)		3.3
Quinolones			
Fluoroquinolones	Levofloxacin	23.5	79.5
	Gemifloxacin		11.3
	Ciprofloxacin/ofloxacin		9.2
Macrolides			15.6
Tetracyclines			0.5
Others			1.5

The frequency and the classes of prescribed antibiotics as well as duration according to the clinical diagnosis of patients are shown in **Tables 3, 4** and **5**.

It should be noted that the amoxicillin-clavulanic acid is frequently prescribed during tonsillitis (15.6%), viral or streptococcal infections, and acute bronchitis (33.8%), usually viral infections. The fluoroquinolones are more frequently prescribed for exacerbation of COPD.

Except for acute bronchitis, antibiotic prescription was evaluated during the other infections to check if it was appropriate or not to the bacteria thought to be responsible, to the mechanisms of resistance and known resistance of bacteria based on local epidemiological data. In most cases, the combination was considered as not justified. Thus, the antibiotic treatment was considered as inappropriate in 88/207 (42.5%) prescriptions **(Table 6)**. The two main causes were the prescription of amoxicillin-clavulanic acid during tonsillitis, non-antipneumococcal fluoroquinolones, when streptococci or streptococcus pneumoniae are presumed to be responsible for infection (between tonsilitis and acute maxillary sinusitis, pneumonia), and unnecessary combination of antibiotics. **(Table 7)**

A group of at-risk patients including 79 people (21.9%) aged 65 and more and/or with diabetes and/or heart failure and/or immune suppression was identified. Among these patients, 50.6% had acute bronchitis, 25.3% exacerbation of COPD, 20.3% tonsillitis, 7.6% pneumonia, 2.5% otitis and 1.3% other infections.

Three hundred and sixty-five patients (365, 97.6%) received a concomitant treatment. The prescribed drugs were antipyretics (71.4%), corticosteroids (44.7%), mucolytic (30.2%), non-steroidal anti-inflammatory (12.3%) and antitussives (8.3%).

Table 3. Frequency of the prescribed antibiotics according to clinical diagnosis of patients.

	Number of patients	Prescribed antibiotics	
		Number	%
One clinical feature	330	319	96.6
Acute bronchitis	116	113	97.4
Tonsillitis	99	92	92.9
Acute maxillary sinusitis	57	56	98.2
Exacerbations of COPDs	28	28	100
Pneumonia	16	16	100
Acute otitis media	12	12	100
Others	2	2	100
More than one diagnosis	44	41	93.2

Table 4. Antibiotic prescription practices during respiratory infections.

	Penicillins	C2G	C3G	Tetracyclines	Macrolides	Fluoro-quinolones	Two antibiotics or more
	%	%	%	%	%	%	%
Diagnostic items							
One clinical feature	42.5	11	6	0.6	15.1	22.3	2.4
Acute bronchitis	38.9	5.3	2.7	1.8	17.7	31.9	1.8
Tonsillitis	45.7	18.5	16.3	0	17.4	1.1	1.1
Acute maxillary sinusitis	42.9	21.4	1.8	0	10.7	21.4	1.8
Exacerbations of COPDs	35.7	0	0	0	0	60.7	3.6
Pneumonia	43.8	0	0	0	18.8	25	12.4
Acute otitis media	72.7	0	0	0	18.2	9.1	0
Others	0	0	0	0	50	0	50
More than one diagnosis	29.3	7.3	2.4	0	22	31.7	6.8
Total	40.9	10.6	5.6	0.6	15.9	23.4	3.1

C2G: Second generation cephalosporin, C3G: third generation cephalosporin.

Table 5. The antibiotics prescribed during ENT and respiratory infections.

	One diagnosis	AB	Tonsillitis	AMS	Exacerbations of COPDs	Pneumonia	AOM	Others	More than one diagnosis	Total
	n=319	n=113	n=92	n=56	n=28	n=16	n=12	n=2	n=41	n=374
	%	%	%	%	%	%	%	%	%	
Penicillin V	0.6	0.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
Co-amoxiclav	30.3	33.6	10.1	42.1	39.3	43.8	66.7	50.0	25.0	29.7
Cefuroxime	10.9	6.0	17.2	21.1	0.0	0.0	0.0	0.0	9.1	10.7
Cefpodoxime	5.5	1.7	15.2	1.8	0.0	0.0	0.0	0.0	2.3	5.1
Cefixime	0.6	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
Azithromycin	3.3	1.7	8.1	0.0	0.0	6.3	0.0	0.0	2.3	3.2
Clarithromycin	8.2	12.9	5.1	7.0	0.0	12.5	0.0	50.0	11.4	8.6
Ofloxacin	20.9	29.3	1.0	19.3	60.7	31.3	8.3	0.0	25.0	21.4
Ciprofloxacin	2.1	3.4	1.0	0.0	7.1	0.0	0.0	0.0	2.3	2.1
Levofloxacin	18.2	25.9	0.0	17.5	53.6	31.3	0.0	0.0	20.5	18.4
Gemifloxacin	1.2	1.7	0.0	1.8	3.6	0.0	0.0	0.0	4.5	1.6
Tetracyclines	0.6	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
Combinations of 2 or more antibiotics	2.4	1.7	1.0	1.8	3.6	12.5	0.0	50.0	6.8	2.9

AB: Acute bronchitis, AOM: Acute otitis media. AMS: Acute maxillary sinusitis. Exacerbations of COPD: Chronic obstructive pulmonary disease. Co-amoxiclav: amoxicillin - clavulanic acid.

Table 6. Frequency of the inappropriate antibiotic treatment.

Clinical items	Number	%
Tonsillitis	30/92	32.6
AMS	22/56	39.3
AOM	5/12	41.7
Exacerbation od the COPD	23/28	82.1
Pneumonia	8/19	42.1

Table 7. Duration of the treatment according to the clinical diagnosis.

	Average duration	Median
	days	days
Tonsillitis	6.2 ± 1.7	6
Acute otitis media	8.3 ± 3	8
Acute maxillary sinusitis	7.7 ± 1.4	8
Pneumonia	9.1 ± 2.3	10
Acute bronchitis	7.2 ± 1.7	7
Exacerbations of COPDs	8.4 ± 1.9	8

Among the 374 eligible patients, 363 (97.1%) were present at the second visit (V2) after an average of 8.1 days (median: 7 days ± 4.6).

The outcome was favorable with improvement or recovery in (91.7%). While in 26 cases (7.1%), there was either a worsening or lack of improvement. In 15 cases (4%), the outcome could not be determined.

The analysis of outcome based on the location of the infection shows clinical success rates ranging from 78.9% in case of pneumonia to 90.7% in case of acute bronchitis.

The recovery rate tends to be nearly significantly higher in patients under 30 years (65.2%) than in those aged 60 and more (32 %) (p = 0.05). Furthermore, the proportion of treatment failure tends to increase significantly with age, from 4.5% in patients under 30 years to 12.5% among those 60 years and older (p = 0.05).

The total average cost of an infectious episode was 79.776 ± 36.988 TND (about 45 ± 20 USD)., with a minimum and maximum values respectively 19.5 and 315.5 TND.

There are significant variations according to the clinical diagnosis. The lowest average cost was observed in tonsillitis, 59.975 TND, while it exceeded 80 TND in acute otitis media, acute maxillary sinusitis, pneumonia and acute exacerbation of chronic obstructive pulmonary disease-COPD.

Discussion

This study showed that tonsillitis, acute maxillary sinusitis and acute bronchitis account for over 90% of ENT and respiratory tract infections. Tonsillitis and acute maxillary sinusitis are significantly more frequent among the young patients, while the frequency of acute bronchitis increases significantly with age.

The approach to diagnosis adopted by GPs was mainly clinical but additional tests were prescribed in 20% of patients. No microbiological tests were conducted which did not allow the identification of bacteria responsible for infection and its susceptibility to antibiotics.

This study highlights the frequency of antibiotics prescription (96.2%) during supposed viral infections such as acute bronchitis, tonsillitis or when antibiotic prescription has to be debatable such as in acute otitis media, sinusitis maxillary or exacerbations of COPD.

An antibiotic treatment was prescribed in 92% of cases of tonsillitis while according to epidemiological data about 80% are of viral origin.

The high frequency of antibiotic prescription is explained by the practitioner's concern to prevent acute rheumatic fever and the lack of availability of rapid diagnostic tests (RDTs) for group A streptococci.

The cost of RDT would be around 3 TND (1.7 US$). RDTs use for diagnosis of bacterial tonsillitis reduces cost and risk of bacterial resistance based on data from a recent study showing that RDT was positive only in 33% of cases of tonsillitis [10]. If a RTD was conducted in 125 cases of tonsillitis, 74 antibiotic prescriptions could be avoided leading to 21% reduction in the cost and preserving the bacterial ecology.

These data should encourage health policy makers to recommend this rapid test as a useful tool in the diagnosis of streptococcal tonsillitis. This study also note the high frequency of macrolides prescription for tonsillitis (26.7%) despite the high rate of *Streptococcus pyogenes* macrolide resistance in Tunisia (22.4%) [11].

Although the abstention of antibiotic treatment is the rule in acute bronchitis in healthy adult, the prescription rate reached 97.1%. The avoidable cost of an antibiotic treatment could be 3471.2 TND (1930 US$).

Exacerbations of COPD are the most expensive respiratory infections in terms of antibiotic treatment, additional tests and concomitant treatments are required. In this study, the antibiotic treatment was systematically prescribed during exacerbations of the COPD and could have been avoided in 5 cases (Grade 0 of COPD) for an avoidable cost of 157.245 DT (87 USD$).

This study confirms that general practitioners tend to prescribe antipyretics (71.4%) and corticosteroids (44.7%).

Overall, this study has clarified the prescribing patterns of antibiotics in the ENT and respiratory tract infections characterized by over-prescribing and unnecessary additional costs related to the lack of diagnostic tools or excessive fear of complications. However, it is important to take in account some limitations of the study, the results are representative for GPs working in the center region of Tunisia and who had agreed to participate in this study and for the patients within the same region. On the other hand, there is a risk of bias due to the fact that GPs may change their practice habits du-

ring the study and adopt a positive attitude to meet the recommendations of correct use of antibiotics. This study did not have bacteriological data making it difficult to distinguish between a viral infection and a bacterial infection.

The over-use of antibiotics is also a concern in developed countries having guidelines for rational use of antibiotics and may lead to emergence of bacterial resistance [3, 12, 13].

In case of presumed viral infection, antibiotics are useless. A recent study showed that strategies of no prescription or delayed antibiotic prescription during acute respiratory tract infections are associated with less strong beliefs in antibiotics and similar symptomatic outcomes to immediate prescription [14].

Patients' knowledge and expectations may influence prescription of antibiotics and « patient information leaflets » could help for awareness and to facilitate consultations witch could be useful to decrease unnecessary prescribing of antibiotics [15].

Conclusion

This study provides real-life data about the clinical practices and antibiotic prescriptions for out patients with ENT and respiratory infections. It shows that GPs have been rarely used laboratory tests to confirm the diagnosis and widely prescribed antibiotics for presumed viral infections.

This study may serve to set up national guidelines for appropriate antibiotic use in order to reduce unnecessary antibiotic prescription and emerging of bacterial resistance.

Working group

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Conflict of Interest

The authors Does not declare a conflict of interest.

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