



Lower respiratory tract infections in adults: non-antibiotic prescriptions by GPs

C. Raherison^{a,*}, R. Poirier^b, J.P. Daurès^c, P. Romand^d, J.P. Grignet^d, P. Arsac^e, J.M. Tartavel^f, D. Touron^g, A. Taytard^a

KEYWORDS

Lower respiratory tract illness; Antibiotics; Pharmaco-epidemiology; Pneumonia; Acute bronchitis; COPD exacerbation; Prescription Summary Background: The AIR II study is a prospective multicentre assessing management of lower respiratory tract infections (LRTIs) in adults by general practitioners (GPs). Epidemiological studies generally address the prescriptions of antibiotics. To our knowledge, little is known about the real impact of non-antibiotic therapeutic prescriptions (defined here as co-prescriptions) in LRTI. Therefore, the aim of the study was to evaluate non-antibiotic prescriptions in LRTIs. Methods: Two thousand general practitioners (GPs) were randomly selected and asked to participate in each of 30 predefined areas covering mainland France. The patient's sociomedical record was completed by the GP during the consultation and sent to the data processing centre at the same time as an anonymous copy of his prescription. The GP also had to report the inclusion by telephone and agree to a telephone appointment with an interviewer. Results: GPs (n = 3144) reported 5469 evaluable cases. Pneumonia accounted for 9.6% of diagnoses, acute exacerbations of chronic bronchitis 14.9% and acute bronchitis 72.5%. Antibiotics were prescribed to 96.5% of patients. In addition to the 5270 prescriptions of antibiotics, co-prescriptions proved to be twice as numerous as prescriptions of antibiotics (10,027 prescriptions for 5115 patients). Mucomodifiers, steroidal anti-inflammatory drugs and bronchodilators were significantly more prescribed in AECB than others. Non-steroidal antiinflammatory drugs and antitussives were significantly more prescribed in acute bronchitis than AECB or CAP. Conclusions: Our results suggest that recommendations of management in LRTIs need to take into account co-prescriptions.

© 2003 Elsevier Ltd. All rights reserved.

Introduction

Episodes of lower respiratory tract infections (LRTI) are the most common reason for consulting a general practitioner (GP). LRTI are frequent and generally include community-acquired pneumonia (CAP), exacerbation of chronic bronchitis (ECB), acute bronchitis (AB). LRTI are a major health care and economic problem due to their high morbidity

E-mail address: chantal.raherison@chu-bordeaux.fr (C. Raherison).

^aHopital du Haut Lévêque, Bordeaux, France

^bCentre Hospitalier du Pays d'Aix en Provence, France

^cInstitut Universitaire de Recherche Clinique, Montpellier, France

^dCentre Hospitalier de Denain, Denain, France

^eHopital d'Orléans, Orléans, France

^fL'espace médical, Trevoux, France

^gLaboratoire Aventis, Paris, France

^{*}Corresponding author. Hopital du Haut Leveque, Centre Francois Magendie 5 avenue de Magellan, Pessac 33604, France. Fax: \pm 33-556556547

996 C. Raherison et al.

and to the direct and indirect costs that their management engenders.² They are usually treated by antibiotics, although guidelines and recommendations suggest reducing the total volume of antibiotic prescription.³ Likewise, epidemiological studies are generally focused on supplementary investigations and on the prescriptions of antibiotics.^{4,5} While patients' complaints such as fever, cough, sputum and dyspnoea lead to symptomatic treatment prescription by GPs in addition to antibiotics, little is known about the real magnitude of non-antibiotic therapeutic prescriptions (defined here as co-prescriptions) in LRTI.

The aim of the study was to evaluate management of LRTI, focusing on non-antibiotic prescription in a large sample from general practice.

Methods

Study design

The methodology of the study has previously been reported. ⁶ The AIR II study was conducted between November 1997 and April 1998. Two thousand general practitioners (GPs) were randomly selected and asked to participate in each of 30 predefined areas covering mainland France. The goal was to obtain a representative sample of at least 200 GPs per area. Some regions were pooled in terms of geographical proximity into the major regions⁷: North, Brittany, South-West, South-East, Centre, North-East and Ile de France. The GPs' participation was voluntary. Their demographic data, year of qualification and the characteristics of their practice were obtained by means of a telephone call from the data processing centre.

Each GP had to include the first two patients diagnosed as suffering from LRTI and being seen for the first time for the current episode, aged between 15 and 65 years and free from cancer, bronchiectasis, hemopathy or tuberculosis. They had to be HIVnegative. Pregnant women were also excluded.

The patient's sociomedical record was completed by the GP during the consultation and sent to the data processing centre at the same time as an anonymous copy of his prescription. The GP also had to report the inclusion by telephone and agree to a telephone appointment with an interviewer. A telephone questionnaire enabled the investigator to collect specific information about the patient, the supplementary procedures prescribed by the GP and the reason for his choices. The interview was conducted on the basis of closed or multiple-choice questions (reason for consultation,

diagnostic criteria, type of LRTI and auscultatory symptoms) without any prior recall of the symptomatological features usually associated with the diagnoses. It also included open questions about the prescriptions of investigations and treatment, work exemption or follow-up appointments. The characteristics of severity, such as respiratory or heart rate, were not recorded insofar as previous experience had shown that they were not usually recorded during the consultation. Crackles means focal signs on chest examination, in favour of pneumonia. Rhonchi was the bronchial manifestation of sputum.

Statistical analysis

The "GP" and "patient" files were analysed separately. Descriptive analyses were undertaken on each form and were expressed as a percentage for qualitative variables and as a median for quantitative variables. Qualitative variables or those converted to qualitative variables were analysed with respect to explanatory data relating to the patients by a bivariate analysis using a χ^2 or Fischer's test. The quantitative variables were analysed by comparing the means using ANOVA methods if applicable and by the Kruskall–Wallis test otherwise. A significance level of 5% was adopted. The calculations were performed using BMDP software version 1993 and Digital 8300 hardware.

Results

General practitioners

A more homogeneous distribution was obtained with 5.6–9.2% of GPs in the sample from each of these seven major regions. The practice locations (rural and semi-rural or town $<\!30,\!000$ or $>\!30,\!000$ inhabitants) were each represented by about a third of the medical population without any bias in terms of the GPs' age and gender.

Three thousand one hundred and forty-four GPs including at least one patient suffering from LRTI participated in the survey. There was no difference between their demographic characteristics and those published in the national statistics from the National Health Insurance Fund.⁸

Patients

Five thousand nine hundred and ninety-eight patients' records were received, 99 of which

contained no sociomedical data and 420 failed to meet the inclusion criteria; 5469 records were therefore included in the analysis. 84.8% of patients had additional medical insurance and all had basic social insurance cover, involving the general scheme in 84.1% of cases, the agricultural scheme in 6.5% and the craftsmen and tradesmen's scheme in 4.2% (vs. 85%, 10% and 5%, respectively, according to national statistics).

Consultations accounted for 73.6% of contacts and visits 26.4%. The reasons for consultation, complaints reported by patients and auscultatory symptoms are presented in Table 1, excluding 214 cases diagnosed as nose infections, so 5354 records were included.

Co-prescriptions according to patient' complaints

In addition to the 5270 prescriptions of antibiotics, multiple co-prescriptions were commonplace (10,027 prescriptions for 5115 patients). Co-prescriptions proved to be twice as numerous as prescriptions of antibiotics. Mucomodifiers repre-

Table 1 Reasons for consultations, patients' complaints, and prescriptions (n = 5354).

Reason for consultation	N (%)
Rhinopharyngeal respiratory	989(18.5)
symptoms	
Bronchopulmonary respiratory	4478(79.9)
symptoms	
Infectious symptoms	1073(20.0)
Constitutional symptoms	819(15.3)
Patients' complaints	
Fever	3592(67.1)
Dyspnoea	1270(23.7)
Cough	4711(88)
Sputum	2895(54.1)
Chest pain	640(12)
Other	230(4.3)
Auscultatory symptoms ($n = 4497$)	
Rhonchi	3663(81.5)
Wheezing	1093(24.3)
Crackles	733(16.3)
None	730(16)
Prescriptions	
Referral to specialist opinion	66(1.2)
Hospitalisation	29(0.5)
Supplementary investigations	579(10.8)
Sick leave	1312(24.5)
Follow-up appointment	1330(24.8)
Antibiotic	5165(96.5)
Co-prescriptions (at least one)	5115(95.5)

sents 32.9% (n=3299) of co-prescriptions, nonsteroidal anti-inflammatory drugs 31.9% (n=3198), antitussives 14.7% (n=1473), Bronchodilators 3.7% (n=376), rhinitis treatment 13.9% (n=1395), and others treatments as homeopathy 2.7%.

In case of antibiotics, prescription was significantly higher in patients aged of 45 years old (97.3%) and more compared with patients < 45 years old (95.6%, P = 0.0007). There was no effect of age of GP's (P = 0.32). In the same way, respiratory comorbidity has no effect on antibiotic prescription (P = 0.28). Prescriptions were lower in Brittany, North-East, and, South-West (respectively, 94.9%, 94.8%, 94.9%) than other centers North, South-East, Centre, and Ile de France (97.5%, 97.8%, 97%, 97.4%, P = 0.0001).

In case of co-prescriptions, we did not find any significant effect of age, comorbidity or geographic difference on prescription.

Mucomodifiers were significantly associated with presence of sputum (Table 2). Non-steroidal anti-inflammatory drugs (NSAID) were associated with fever. Steroidal anti-inflammatory drugs (SAID) and bronchodilators were associated with dyspnoea, and antitussives were significantly associated with chest pain.

Co-prescriptions according to auscultatory symptoms

Mucomodifiers were significantly associated with rhonchus and NSAID were associated with crackles. SAID and bronchodilators were associated with wheezing (Table 3).

Co-prescriptions according to GP' diagnosis

Mucomodifiers, SAID and bronchodilators were significantly more prescribed in AECB than others. NSAID and antitussives were significantly more prescribed in AB than in AECB or CAP (Table 4).

Discussion

This study represents a new step in analysing the reasons for non-antibiotic prescriptions by GPs by placing them in their usual symptomatological and sociomedical context. Its originality lies in the fact that symptoms, supplementary diagnostic procedures, treatment and sociomedical parameters likely to influence prescriptions, were collected for the same patients. In addition, these details were recorded in real time from authentic cases to

998 C. Raherison et al.

Medications	Fever, N = 3434 N (%)	Cough, N = 4507 N (%)	Sputum, N = 2744 N (%)	Dyspnoea, N = 1208 N (%)	Chest pain, N = 608 N (%)
Mucomodifiers	2146(62.5)	2830(62.3)	1915(69.8) ^a	784(64.9)	365(60)
NSAID	189(53.6)	2120(47.1)	1197(43.6)	467(8.6) ^a	318(52.3)
SAID	479(14)	646(14.3)	40(14.7)	381(31.5) ^a	116(19)
Antitussives	898(26.2)	1233(27.4)	606(22.1)	254(21)	178(29.3)a
Bronchodilators	187(5.4)	277(6.1)	185(6.7)	202(16.7) ^a	32(5.3)

Medications	Rhonchus,	Wheezing,	Crackles,
	<i>N</i> = 3486	<i>N</i> = 1053	<i>N</i> = 703
	N (%)	N (%)	N (%)
Mucomodifiers	2356(67.6) ^a	659(62.6)	460(64.5)
NSAID	1548(44.4)	363(34.5)	336(47.1)
SAID	523(15)	392(37.3) ^a	125(17.5)
Antitussives	830(23.8)	253(24)	171(24)
Bronchodilators	249(7.1)	225(21.4) ^a	44(6.2)

Medications	Pneumonia,	Acute exacerbation	Acute bronchitis	
	n = 496	of chronic bronchitis, $n = 762$	n = 3656	
	N ^b (%)	N ^b (%)	N ^b (%)	
Mucomodifiers	292 (59.5)	539 (71) ^a	2329 (62.7)	
NSAID	225 (45.8)	246 (32.5)	1813 (48.9) ^a	
SAID	93 (18.9)	202 (26.6) ^a	456 (12.3)	
Antitussives	122 (24.8)	143 (18.8)	1040 (28) ^a	
Bronchodilators	21 (4.3)	116 (15.3) ^a	194 (5.2)	

prevent the bias introduced by declarative or retrospective studies. Three thousand one hundred and forty-four GPs agreed to take part voluntarily and 5469 cases were analysed. The initial calculation of a representative sample was based on the frequency of antibiotic prescriptions in 80% of cases, a figure which was exceeded. It also aimed to achieve a homogeneous distribution of the population of GPs across the seven predefined areas, an objective not reached for all of them. However, the distribution of GPs and patients was relatively homogeneous across the country. In addition, the comparison between the sample of GPs and the general medical population, as listed

by the National Health Insurance Fund, means that the sample may be considered as representative on a national scale. Likewise, the demographic data of the patients and the respective proportions of the various health insurance funds, which were very similar to the national data, are also indicative of their representativeness. It cannot be ruled out that the first two LRTI patients consulting their GP were not in fact included, so a selection bias is possible. However, this is the case in all studies using this kind of methodology. Moreover, because the aim of the study was to evaluate the approach of GPs' pragmatically, any bias would only have a limited influence on the results.

Mucomodifiers are by far the most common coprescriptions, involving 70% of patients with sputum and thus 60% of LRTI. The long experience gained with these products means that their safety is no longer in doubt, even though a literature review in 1993 failed to find any solid evidence of their value. However, a meta-analysis evaluated the effects of oral mucolytics in adults with stable chronic bronchitis or COPD, and concluded in a small reduction in acute exacerbations and a somewhat greater reduction in total number of days of disability. 10 In our study, no questions were asked the GPs about bronchopulmonary hygiene physical therapy prescribed. Bronchopulmonary hygiene therapy is a form of chest physical therapy including chest percussion and postural drainage to remove lung secretions. It is commonly used in patients with both acute and chronic airway diseases. A recent review concluded in the absence of evidence to support or contraindicate the use of this physical therapy in people with chronic obstructive pulmonary disease and bronchiectasis. 11

NSAID were prescribed for fever and chest pain significantly more frequently compared with other complaints. About one patient in five had wheezing, an auscultatory symptom which, even more than dyspnoea, was the main reason for prescribing a steroid or a bronchodilator. Like the prescriptions of steroids and bronchodilators, both signs are very frequent in ECB. In addition, obvious or suspected asthma may be a reason for prescribing steroids and bronchodilators. Steroid prescription was significantly higher for dyspnoea, wheezing, and exacerbation of chronic bronchitis compared with other groups. However, only 27% of EACB received steroid prescriptions. This result highlights the lack of steroid prescription in this case. GPs needs to get more information about management of EACB, particularly steroids use. In addition, unfortunately, information on reaction of patient behind this prescription was not available in our study.

However, AB accounted for a considerable proportion of these prescriptions (96.5%), in most cases macrolides (37.1–44.8%), aminopenicillins (6.3–30.1%), and for others, cephalosporins, quinolones and synergystins. The possibility of expiratory suppression in reaction to the irritation of the bronchial nerve endings is known in AB,¹² although its incidence has not precisely been evaluated. Nevertheless, 19% of SAID in pneumonia is very surprising but may be due to presence of thoracic pain.

The prescription of antitussives is frequent. GPs used them less in cases of ECB, an approach that is consistent with the recommendations, although the

proportion was too high (20%).¹³ However, their symptomatic efficacy is questionable when coughing is the result of an acute infection.⁹ Likewise, the lack of any drawbacks is doubtful in all cases in which a cough is thought to be useful (i.e. when it is productive), even outside the setting of an ECB.

In conclusion, this study highlights the volume of prescriptions (both antibiotics and co-prescriptions) in response to LRTI. Despite existing recommendations to reduce or improve antibiotics prescription, there is no evidence-based medicine for prescriptions for symptomatic treatments. Non-antibiotic prescriptions appeared to be linked to the degree of the symptoms, each of which tended to receive an individual therapeutic response. Our results suggest that evidence-based medicine recommendations are needed for utilization of co-prescriptions in management of LRTI's in general practice.

Acknowledgements

The study was sponsored by the Société de Pneumologie de Langue Française and the Société de Pathologie linfectieuse de Langue Française, and was supported by Laboratoire Aventis Pharma France. The authors are grateful to Doctor François Elkik for his assistance in preparing the manuscript and to Ray Cooke for assistance with the manuscript.

References

- Macfarlane J, Macfarlane R, Holmes W. Contemporary use of antibiotics in 1089 adults presenting with acute lower respiratory tract illness in general practice in the UK: implications for developing management guidelines. Respir Med 1997;91:427–34.
- Macfarlane JT, Colville A, Guion A, Macfarlane RM, Rose DH. Prospective study of aetiology and outcome of adult lower respiratory tract infections in the community. *Lancet* 1993;341:511–4.
- ERS Task Force Report. Guidelines for management of adult community-acquired lower respiratory tract infections. Eur Respir J 1998;11:986–91.
- Woodhead M, Gialdroni-Grassi G, Huchon GJ, Léophonte P, Manresa F, Schaberg T. Use of investigations in lower respiratory tract infection in the community: a European survey. Eur Respir J 1996;9:1596–600.
- Huchon GJ, Gialdroni-Grassi G, Léophonte P, Manresa F, Schaberg T, Woodhead M. Initial antibiotic therapy for lower respiratory tract infection in the community: a European survey. Eur Respir J 1996;9:1590–5.
- Raherison C, Peray P, Poirier R, Romand P, Grignet JP, Arsac P, Taytard A, Daures JP. Management of Lower Respiratory Tract Infections by French General Practitioners The AIR II study. Eur Respir J 2002;19:1–6.

1000 C. Raherison et al.

- Taytard A, Daurès JP, Arsac P, et al. Analyse de la prise en charge des infections respiratoires basses en médecine générale. Rev Mal Resp 2001;18:163–70.
- 8. Caisse Nationale d'Assurance Maladie (CNAM) sn. Personal communication.
- Irwin RS, Curley FJ, Bennett FM. Appropriate use of antitussives and protusives, a practical review. *Drugs* 1993; 46(1):80–91.
- Poole PJ, Black PN. Mucolytic agents for chronic bronchitis (Cochrane Review). In: The Cochrane Library, Oxford: update software 1, 2002.
- 11. Jones AP, Rowe BH. Bronchopulmonary hygiene physical therapy for chronic obstructive pulmonary disease and bronchiectasis (Cochrane Review). In: The Cochrane Library, Oxford: update software 1, 2002.
- 12. Gonzales R, Sande MA. Uncomplicated acute bronchitis. *Ann Int Med* 2000;133:981–91.
- SPLIF. Révision de la IVème conférence de consensus en thérapeutique anti-infectieuse de la Société de Pathologie Infectieuse de Langue Française. Med Mal Infect 2000; 30:565–80.