Ong, D.S.Y., Kuyvenhoven, M.M., Dijk, L. van, Verheij, T.J.M. Antibiotics for respiratory, ear and urinary tract disorders and consistency among GPs. Journal of Antimicrobial Chemotherapy: 2008, 62(3), 587-592

Antibiotics for respiratory, ear, and urinary tract disorders and consistency among GPs

DAVID S.Y. ONG*, MARIJKE M. KUYVENHOVEN, LISET VAN DIJK, THEO J.M. VERHEIJ

*corresponding author
David S.Y. Ong BSc, pharmacy and medical student, davidsyong@gmail.com
Marijke M. Kuyvenhoven PhD, senior lecturer, M.M.Kuyvenhoven@umcutrecht.nl
Theo J.M. Verheij PhD, professor of General Practice, T.J.M.Verheij@umcutrecht.nl
Julius Center for Health Sciences and Primary Care
University Medical Center (UMC) Utrecht, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands Phone number: +31 30 253 8198 Fax number: +31 30 253 9028

Liset van Dijk PhD, l.vandijk@nivel.nl
Netherlands Institute for Health Services Research (NIVEL) Otterstraat 118-124, 3513 CR Utrecht, the Netherlands Phone number: +31 30 272 9700 Fax number: + 31 30 272 9729

Objectives. To describe the specific diagnoses for which systemic antibiotics are prescribed, to assess adherence of antibiotic choice to national guidelines, and to assess consistency among GPs in prescribed volumes of antibiotics for respiratory, ear and urinary tract disorders.

Methods. A cross-sectional study including 174 GPs from 89 general practices. Data were derived from the Second Dutch National Survey of General Practice (DNSGP-2) in 2001. Outcome measures were the antibiotic prescriptions for respiratory, ear, and urinary tract disorders defined according to ICPC codes, the percentage of first-choice antibiotics complying with national guidelines, and the number of antibiotic prescriptions per 1000 patients per GP per year.

Results. Most antibiotics for respiratory tract disorders were prescribed for acute bronchitis (25%), sinusitis (22%) and acute upper RTI (14%). Most antibiotics were prescribed for acute otitis media (77% of ear disorders) and for cystitis (95% of urinary tract disorders). First-choice antibiotics were prescribed in about 75% of cases, while macrolides and amoxicillin-clavulanate (being second-choice antibiotics) were prescribed in about 25%, especially in lower respiratory tract infections. The correlations (Spearman rho) between prescribed volumes for the three main groups of disorders varied from 0.39 to 0.67.

Conclusions. GPs were consistent in prescribing antibiotics for the three groups of diseases. Improvement strategies should focus on the management of acute upper RTIs and acute bronchitis and also on the use of amoxicillin-clavulanate and macrolides, these being mostly second-choice antibiotics in national guidelines.

INTRODUCTION

About 85% of outpatient antibiotic prescriptions are prescribed by general practitioners (GPs).[1] Although the Netherlands has the lowest outpatient antibiotic prescription rate in Europe,[2] there are two aspects that are of concern. Firstly, about 50% of antibiotic prescriptions for respiratory tract infections (RTIs) are not in accordance with national guidelines.[3,4] This causes unnecessary expenditure and use of health services, encouraging patients to re-consult their GP for subsequent similar problems, unnecessary side effects, and the possible development of antibiotic resistance.[1,2,5-7] Secondly, the international trend of a decline in the use of narrow-spectrum and older penicillins and of prescribing more broad-spectrum and new antibiotics has also been shown to exist in low-prescribing countries such as the Netherlands.[1,8] This last group of antibiotics should only be used in more severe infections or in case of intolerance of first-choice antibiotics.

Although still low, there is an increase in bacterial resistance in the Netherlands.[8,9] In *Escherichia coli* resistance rates for trimethoprim and amoxicillin have increased from 10% and 20% in 1997 to 22% and 32% in 2003-2004, and resistance to macrolides among clinical isolates of *Streptococcus pneumoniae* is about 8%.

Recently we have shown that in the Netherlands about 50%, 7% and 25% of all systemic antibiotic prescriptions in general practice are prescribed for respiratory, ear and urinary tract disorders respectively,[10] but till now it is unknown for which specific diagnoses these antibiotics are prescribed. This study aimed to describe the specific diagnoses for which systemic antibiotics are prescribed, to assess the degree to which Dutch GPs adhere to national guidelines concerning antibiotic choice in cases of sinusitis, tonsillitis, lower RTIs, acute otitis media and urinary tract infections, and to assess consistency in prescribing antibiotics. More insight into these aspects may contribute to strategies and interventions to improve antimicrobial management in general practice.

[TABLE 1]

METHODS

GPs, setting and data collection

Morbidity and antibiotic prescription data were collected from the Second Dutch National Survey of General Practice (DNSGP-2).[11] This survey included 195 GPs in 104 practices serving 400,912 patients (mid-time population). For this study 15 out of the 104 practices were excluded because of inadequate registration of contacts and/or prescriptions, and software problems in registration. Our study population therefore consisted of 89 practices, 174 GPs and 356,178 patients (mid-time population). The characteristics of the study group as well as those of the original sample of participating GPs did not differ from those of the total population of Dutch GPs and patients, except for type of practice, in that single handed practices were underrepresented.[11]

Data were derived from electronic medical records during a one-year period. Data on morbidity included the indication in International Classification of Primary Care version 1 (ICPC-1) format, dates and patient identification. Drugs were coded according to the World Health Organization (WHO) Anatomical Therapeutical Chemical (ATC) classification.[12]

Outcome measures were (a) the antibiotic prescriptions for respiratory, ear, and urinary tract disorders according to ICPC codes, (b) the percentage of first-choice antibiotics according to national guidelines, and (c) the number of systemic antibiotic (=J01 ATC code) prescriptions per 1000 patients per GP per year for all cases and according to respiratory, ear and urinary tract disorders.

Analysis

After calculating distributions of the number of antibiotic prescriptions per 1000 patients per GP among ICPC chapters and the most frequently used ICPC codes, adherence to national recommendations concerning antibiotic choice as available from national GP guidelines in 2001 (Table 1) was analysed.[13-17] To assess to which degree GPs were consistent in prescribing antibiotics, Spearman correlation coefficients (rho) were calculated between the numbers of antibiotic prescriptions per 1000 patients per year for respiratory, ear and urinary tract disorders. Data were analysed with the Statistical Package for Social Sciences (SPSS) version 13.0.1 for Windows.

RESULTS

In total 85,274 systemic antibiotic prescriptions were prescribed to 53,036 patients with a mean age of 43 years and 64% being female. About 15% of the patients received at least one antibiotic prescription during a one-year period, with an average of 1.6 prescriptions per patient. The rate of patients getting three or more antibiotic prescriptions per year ranged from 9% in children under five years to 12% in patients between 5 and 64 years, and 20% in patients over 64 years.

Antibiotic prescriptions for respiratory, ear, and urinary tract disorders

Eighty-six percent of the prescriptions were classified with an ICPC code (n=73,246). In 14% of the prescriptions a diagnosis was missing (n=12,028), more frequently for quinolones (22%) compared to other subgroups. Fifty percent of the 73,246 prescriptions were prescribed for respiratory, 7% for ear and 28% for urinary tract disorders. In the group of respiratory tract diseases most antibiotics were prescribed for acute bronchitis (25%) and sinusitis (22%), followed by acute upper RTI (14%) and acute tonsillitis (9%) (Table 2). Almost all antibiotic prescriptions for urinary tract disorders were prescribed for cystitis (95%) and 77% of prescriptions for ear disorders were prescribed for acute otitis media.

[TABLE 2]

Adherence to guidelines

Antibiotic prescriptions for sinusitis and acute tonsillitis corresponded with recommended first-choice antibiotics in 80% and 70% of the prescriptions, respectively (Table 3). About 75% of the prescriptions for acute otitis media and urinary tract infections were first-choice drugs. Prescriptions for acute bronchitis were mostly tetracyclines (41%) and amoxicillin (31%), followed by macrolides (16%) and amoxicillin-clavulanate (9%). Almost half of prescriptions for pneumonia were amoxicillins (26%) or tetracyclines (20%), and the remaining were amoxicillin-clavulanate (24%) and macrolides (23%).

GPs' consistency in prescribed antibiotic volumes

For all cases there was a mean number of 260 (SD 108) antibiotic prescriptions per 1000 patients per GP per year with a median of 244 prescriptions (IQR 195- 333). The median numbers of prescriptions for respiratory, ear and urinary tract disorders were 98 (IQR 60-139), 12 (IQR 7-19) and 60 (IQR 41-77) respectively. There was a high correlation between prescribed volumes of antibiotics for respiratory and ear disorders (Spearman rho: 0.67; $P < 0.001$), which means that GPs who prescribed high volumes of prescriptions for respiratory disorders also prescribed high volumes for ear disorders. The correlations between prescribed volumes for respiratory and urinary tract disorders and between prescribed volumes for urinary tract and ear disorders were moderate (Spearman rho: 0.51; $P < 0.001$, and 0.39; $P < 0.001$ respectively). Multivariate analysis showed that these correlations were not influenced by factors such as differences in age or gender between practices (data not shown).

DISCUSSION

In this survey acute bronchitis, sinusitis and acute upper RTI were the most common respiratory disorders for which antibiotics were prescribed, whereas cystitis and acute otitis media were the most common urinary tract and ear disorders in this respect. About 20% to 30% of antibiotic prescriptions were not the recommended first-choice antibiotics, especially macrolides and amoxicillin-clavulanate for respiratory and quinolones for urinary tract disorders. GPs were fairly consistent in their prescribed volumes of antibiotics for respiratory, ear, and urinary tract disorders.

Strengths and limitations of the study

The DNSGP-2 provides a good representation of morbidity and prescribing habits in Dutch general practice,[11] except for an under-representation of GPs with single-handed practices. Data were assumed to be accurate since extraction took place from electronic medical records of the practices,[18] and inter-observer reliability of coding episodes into the ICPC codes was high.[19] The number of prescriptions was used as outcome measure. It was not possible to use defined daily doses (DDD), since information on the dosage of antibiotics was not often registered by GPs. However, the measure used here has the advantage that it clearly depicts GP's decision to prescribe or not.

[TABLE 3]

The results of the DNSGP-2 on prescription rates for antibiotics generally correspond with the nationwide reimbursement figures.[10] The average number of 1.6 antibiotic prescriptions per patient found in this study was almost the same as the average of 1.7 prescriptions per patient mentioned in the nationwide reimbursement figures.[20] However, GPs participating in this survey prescribed fewer antibiotics than the total population of GPs and especially fewer macrolides and quinolones.[10] GPs voluntarily participating in the research network of the nationwide GP database DNSGP-2, probably adhere more consistently to guidelines than non-participating GPs, leading to higher prescribing of first-choice antibiotics. We thus may assume that our study underestimated the volume of second-choice antibiotics used in Dutch general practice, especially for quinolones for which diagnoses were missing relatively often.

Comparison with existing literature and interpretation of results

Assuming that antibiotics are usually not indicated for acute upper RTI and acute bronchitis, it is likely that in most of these prescriptions, representing 14% and 25% of all antibiotic prescriptions for respiratory tract disorders, either the diagnosis or the indication for antibiotic treatment was incorrect. Recently, this phenomenon was also described for the UK.[21] Comparing the distributions of antibiotics across respiratory tract disorders in both countries, one sees that British GPs prescribe relatively twice as many antibiotic prescriptions for acute upper RTI and acute tonsillitis, while Dutch GPs prescribe twice as many antibiotics for sinusitis as their UK colleagues.[21] These differences might partly be attributed to differences in diagnostic preferences and coding practices between Dutch and British GPs and partly to real differences in antimicrobial management between the UK and the Netherlands. The proportions of antibiotics for lower RTIs are more or less the same in both countries. The number of antibiotic prescriptions for urinary tract disorders in proportion to all antibiotic prescriptions is almost three times higher in the Netherlands than in the UK. This might be partly explained by the higher volume of antibiotics in the UK resulting in a larger denominator of all prescriptions,[2] while we assume that the volume of antibiotics for urinary tract disorders are somewhat similar in both countries. Future studies should use similar denominators such as the number of prescriptions per 1000 patients to make comprehensive comparisons possible.

About three-quarters of antibiotics are first-choice antibiotics. The use of second-choice antibiotics in terms of volume is not yet a major issue in the Netherlands,[22,23] but the increase

from 4% in 1987 [24] to 25% second-choice antibiotics in this study is a reason for concern. More restriction is necessary mainly for the use of amoxicillin-clavulanate and macrolides.

Bacterial resistance cannot be a motive for the use of amoxicillin-clavulanate in community acquired pneumonia (CAP) since *S. pneumoniae* is the most frequent cause of CAP and resistance of *S. pneumoniae* to penicillin and other antibiotics in general practice is low.[8] Because resistance in *Haemophilus influenzae* can be relevant in primary care settings and this pathogen is more prominent in some chronic ill patients, the use of amoxicillin-clavulanate might be considered for patients with co-morbidity like diabetes and chronic obstructive pulmonary disease (COPD). Three-quarters of amoxicillin-clavulanate prescriptions for pneumonia in our study were prescribed for patients without diabetes or COPD. In addition, the prevalence of allergy to penicillin, which is estimated to be between 0.7 and 8%, could not explain the use of second-choice antibiotics like macrolides for common infections.[25]

This study showed that GPs were consistent in their prescribed volumes of antibiotics across respiratory, ear and urinary tract disorders. A consistency in prescribing antibiotics for children (older than 24 months) with acute otitis media, patients with sore throat, patients with sinusitis, children (up to 6 years) with fever, and children (up to 12 years) with asthma has been shown earlier.[26] This consistency corroborates our finding that GP's diagnostic labelling, in addition to the number of acute respiratory tract episodes per 1000 patients, is an independent predictor of the prescribed volume of antibiotics.[27]

Conclusions

Future antimicrobial improvement strategies should focus particularly on the management of acute upper RTIs, acute bronchitis, and the prescription of second-choice antibiotics, notably on the use of amoxicillin-clavulanate and macrolides. While doing this, consistency in antibiotic management of GPs should be taken into account.

ACKNOWLEDGEMENTS

We thank all GPs who voluntarily participated in this study and Peter Zuithoff for his statistical assistance.

FUNDING

The Second Dutch National Survey of General Practice (DNSGP-2) has been funded by the Dutch Ministry of Health, Welfare and Sport.

TRANSPARENCY DECLARATIONS

None to declare.

REFERENCES

1 Kuyvenhoven MM, van Balen FA, Verheij TJ. Outpatient antibiotic prescriptions from 1992 to 2001 in the Netherlands. J Antimicrob Chemother 2003; 52: 675-8.

2 Goossens H, Ferech M, Vander Stichele R et al. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet 2005; 365: 579-87.

3 Akkerman AE, Kuyvenhoven MM, van der Wouden JC et al. Determinants of antibiotic overprescribing in respiratory tract infections in general practice. J Antimicrob Chemother 2005; 56: 930-6.

4 de Melker RA. [Efficacy of antibiotics in frequently occurring airway infections in family practice]. Ned Tijdschr Geneeskd 1998; 142: 452-6.

5 Gonzales R, Bartlett JG, Besser RE et al. Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. Ann Intern Med 2001; 134: 479-86.

6 Wise R. The relentless rise of resistance? J Antimicrob Chemother 2004; 54: 306-10.

7 McCaig LF, Besser RE, Hughes JM. Antimicrobial drug prescription in ambulatory care settings, United States, 1992-2000. Emerg Infect Dis 2003; 9: 432-7.
8 SWAB. Nethmap 2007 – Consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in The Netherlands. 52 pp. http://www.swab.nl (12 May 2008, date last accessed)
9 SWAB. Nethmap 2006 – Consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in The Netherlands. 53 pp. http://www.swab.nl (12 May 2008, date last accessed)
10 Akkerman AE, Kuyvenhoven MM, Verheij TJ et al. Antibiotics in Dutch General Practice: nationwide electronic GP database and national reimbursement rates. Pharmacoepidemiol Drug Saf 2008; 17: 378-83.
11 Westert GP, Schellevis FG, de Bakker DH et al. Monitoring health inequalities through general practice: the Second Dutch National Survey of General Practice. Eur J Public Health 2005; 15: 59-65.
12 WHO Collaborating Centre for Drug Statistics Methodology. http://www.whocc.no/atcddd/ (12 May 2008, date last accessed)
13 De Bock GH, Van Duijn NP, Dagnelie et al. NHG-standaard Sinusitis. Huisarts Wet 1993; 36: 255-7.
14 Dagnelie CF, Zwart S, Balder FA et al. NHG-standaard Acute Keelpijn. Huisarts Wet 1999; 42: 271-8.
15 Appelman CLM, Van Balen FAM, Van de Lisdonk EH et al. NHG-standaard Otitis media acuta. Huisarts Wet 1999; 42: 362-6.
16 Timmermans AE, Baselier PJAM, Winkens RAG et al. NHG-standaard Urineweginfecties. Huisarts Wet 1999; 42: 613-22.
17 van der Kuy A. Farmacotherapeutisch Kompas 2000-2001. Amstelveen: Commissie Farmaceutische Hulp van het College voor zorgverzekeringen, 2000.
18 Thiru K, Hassey A, Sullivan F. Systematic review of scope and quality of electronic patient record data in primary care. BMJ 2003; 326: 1070.
19 van der Linden MW, Westert GP, de Bakker DH et al. Tweede nationale studie naar ziekten en verrichtingen in de huisartsenpraktijk: klachten en aandoeningen in de bevolking en in de huisartspraktijk. [Second Dutch national survey on morbidity and interventions in general practice: complaints and diseases in the population and in general practice; in Dutch]. Utrecht/Bilthoven: NIVEL/RIVM; 2004.
20 The Dutch Drug Information System of the Health Care Insurance Board. http://www.gipdatabank.nl/ (12 May 2008, date last accessed)
21 Petersen I, Hayward AC. Antibacterial prescribing in primary care. J Antimicrob Chemother 2007; 60: Suppl. 1, i43-7.
22 Steinman MA, Landefeld CS, Gonzales R. Predictors of broad-spectrum antibiotic prescribing for acute respiratory tract infections in adult primary care. JAMA 2003; 289: 719-25.
23 Piccirillo JF, Mager DE, Frisse ME et al. Impact of first-line vs second-line antibiotics for the treatment of acute uncomplicated sinusitis. JAMA 2001; 286: 1849-56.
24 Melker RA, Kuyvenhoven MM. Management of upper respiratory tract infections in Dutch family practice. J Fam Prac 1994: 38: 353 -7.
25 Weiss ME, Adkinson NF. Immediate hypersensitivity reactions to penicillin and related antibiotics. Clinical Allergy 1988; 18: 515-40.
26 JCC Braspenning, FG Schellevis, RPTM Grol. Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Kwaliteit huisartsenzorg belicht. [Second Dutch national survey on morbidity and interventions in general practice: quality of care; in Dutch]. Utrecht/Nijmegen: NIVEL/WOK, 2004.
27 van Duijn HJ, Kuyvenhoven MM, Tiebosch HM et al. Diagnostic labelling as determinant of antibiotic prescribing for acute respiratory tract episodes in general practice. BMC Fam Pract 2007; 8: 55.

TABLES

Table 1. First-choice antibiotics according to Dutch national GP guidelines as available in 2001

National guideline*	ICPC code	First-choice subgroup(s)
Sinusitis	Sinusitis (R75)	Tetracyclines
		Amoxicillin
		Sulphonamides and trimethoprim
Acute sore throat	Acute tonsillitis (R76)	Narrow-spectrum penicillins
Lower respiratory tract infection **	Acute bronchitis (R78)	Tetracyclines
		Amoxicillin
		Sulphonamides and trimethoprim
	Pneumonia (R81) ***	Amoxicillin
Acute otitis media	Acute otitis media (H71)	Amoxicillin
Urinary tract infection	Cystitis (U71)	Nitrofurantoin Sulphonamides and trimethoprim

* In 2001 there were four national GP guidelines available concerning antibiotic use for respiratory, ear or urinary tract diseases: 'Sinusitis' [13], 'Acute sore throat' [14], 'Acute otitis media' [15], and 'Urinary tract infection' [16].

** No guideline of the Dutch College of General Practitioners was available for lower respiratory tract infections in 2001, so the recommendations of 'Therapeutic Guidelines' of The Health Care Insurance Board (College voor Zorgverzekeringen, Diemen, The Netherlands) in 2000/2001 was used to determine first-choice antibiotics [17].

*** In case of severe pneumonia parenteral benzylpenicillin is indicated.

Table 2. The volume of antibiotic prescriptions according to respiratory, ear, urinary tract and remaining disorders (n=73,246 prescriptions)

ICPC Chapter / Code		Volume of J01 prescriptions		
		%	absolute	%
Respiratory				
R05	Cough	5.7		
R74	Acute upper respiratory infection	14.2		
R75	Sinusitis	21.9		
R76	Acute tonsillitis	8.9		
R78	Acute bronchitis	24.7		
R81	Pneumonia	6.1		
Remaining R-codes		18.5		
Subtotal		100.0	36280	49.5
Ear				
H70	Otitis externa	9.8		
H71	Acute otitis media	76.6		
Remaing H-codes		13.6		
Subtotal		100.0	4936	6.7
Urinary				
U70	Pyelonephritis / pyelitis, acute	1.6		
U71	Cystitis	94.6		
Remaining U-codes		3.8		
Subtotal		100.0	20461	27.9
Remaining ICPC chapters			11569	15.9
Total			73246	100.0

Table 3. Percentages first- and second-choice or remaining antibiotics according to Dutch national guidelines as available in 2001 (n=73,246 prescriptions)

National guideline	ICPC code	First-choice subgroups	%	Second-choice subgroups/remaining	%
Sinusitis	Sinusitis (R75)	Tetracyclines	57.5	Macrolides	12.3
		Amoxicillin	18.9	Amoxicillin-clavulanate	8.1
		Sulphonamides and trimethoprim	2.4	Other	0.8
Acute sore throat	Acute tonsillitis (R76)	Narrow-spectrum penicillins	69.7	Amoxicillin	13.0
				Macrolides	9.2
				Other	8.1
Lower respiratory tract infection	Acute bronchitis (R78)	Tetracyclines	40.7	Amoxicillin-clavulanate	8.7
		Amoxicillin	31.0	Macrolides	16.1
		Sulphonamides and trimethoprim	2.1	Other	1.4
	Pneumonia (R81)	Amoxicillin	26.4	Tetracyclines	20.3
				Macrolides	22.5
				Amoxicillin-clavulanate	24.0
				Other	6.8
Acute otitis media	Acute otitis media (H71)	Amoxicillin	76.7	Macrolides	8.8
				Sulphonamides and trimethoprim	1.9
				Amoxicillin-clavulanate	8.5
				Other	4.1
Urinary tract infection	Cystitis (U71)	Nitrofurantoin	32.7	Quinolones	13.1
		Sulphonamides and trimethoprim	43.3	Other	10.9