

Antibiotics and steroids for exacerbations of COPD in primary care: compliance with Dutch guidelines

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ABSTRACT

Background

The Dutch College of General Practitioners' guidelines specify that antibiotics should only be used for severe cases of chronic obstructive pulmonary disease (COPD). However, GPs tend to administer antibiotics rather than a short course of steroid treatment regardless of severity.

Aim

The aim of this study was to determine how GPs use current guidelines in treating exacerbations of COPD, in particular whether short courses of oral steroids and antibiotics are prescribed in accordance with the Dutch guidelines for COPD.

Design of study

Retrospective analysis of medical records.

Setting

Primary healthcare centres.

Method

Medical records of patients registered at four primary healthcare centres in the Netherlands were retrospectively analysed for the period March 2001–March 2003.

Results

Of 35 589 patients, 1.3% were registered as having a diagnosis of COPD. In 2 years, 47% of the patients had no exacerbation, 35% had one or two exacerbations, and 18% had three or more exacerbations. Of 536 exacerbations, GPs prescribed a short course of oral steroids in 30% of cases, antibiotics in 29%, steroids combined with an antibiotic in 23%, and no oral steroid course or antibiotic was prescribed in 18%. Prescriptions for patients with three or more exacerbations differed significantly from those for patients with one or two exacerbations.

Conclusions

Treatment is often not in accordance with current guidelines; in particular, antibiotics are prescribed more often than recommended.

Keywords

antibiotics; COPD; exacerbation; primary health care; steroids.

INTRODUCTION

Patients with an acute exacerbation of chronic obstructive pulmonary disease (COPD) can be treated with short courses of systemic corticosteroids and/or with antibiotics. Compared with placebo, a short course of systemic steroids results in a more rapid improvement in flow rate¹⁻³ and dyspnoea score;^{1,2} shorter hospital stay;³ and a decrease in the rate of clinical relapse.¹⁻³ Antibiotic treatment appears to be of the greatest benefit to patients with severe symptoms⁴ and/or a low baseline flow rate.⁵⁻⁶ For mild episodes, no significant advantage of antibiotic treatment has been demonstrated.⁷⁻⁸ In a primary healthcare setting, antibiotic treatment was shown to neither accelerate recovery nor reduce the number of relapses in patients with exacerbations.⁹

The Dutch College of General Practitioners has developed guidelines for the diagnosis and treatment of COPD in general practice.¹⁰ These guidelines state that in the majority of exacerbations treatment with

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bronchodilators is sufficient, but if not, a course of oral steroids (30 mg for 7–10 days) should be prescribed. Antibiotics are advised only in acute severe dyspnoea where there are symptoms of clinical infection, a low baseline flow rate (forced expiratory volume in 1 second [FEV1] <30%), or insufficient recovery after 4 days. Despite wide availability of the guidelines, implementing them is a complex process and it is unclear whether it is viable to apply them in daily practice.

In the Netherlands most patients with exacerbations of COPD are treated by GPs. The aim of this study was to assess whether short courses of steroids and antibiotics are prescribed in accordance with the Dutch guidelines.

METHOD

Patient population

Four primary healthcare centres took part in the study. These centres participate in the GP-based continuous morbidity registration network of the Department of General Practice, Academic Medical Centre – University of Amsterdam. This network registers chronic diseases among other data in electronic medical records (EMRs). For the period March 2001 until March 2003, we retrospectively analysed EMRs of all registered patients at these four centres.

Data collection

Records of all patients registered with a diagnosis of COPD were retrieved from EMRs with the use of the international classification of primary care code (ICPC) R95.¹¹ Consultations for these patients during the 2-year study period were analysed by printing and subsequently reading and coding the EMRs. Two criteria were used to assess an exacerbation of COPD:

- when 'exacerbation' was used by the GP as stated in the EMR; and
- when increased symptoms of COPD (cough, shortness of breath, altered sputum conditions, increased sputum production, wheezing, or illness) were explicitly mentioned in the EMR.

When patients visited their GP for an exacerbation more than once in a period of up to 3 weeks, the whole episode was considered one exacerbation. An exacerbation after full recovery from the previous exacerbation was considered a new episode, according to the GP's description in the EMR, or when the time between two consultations at the GP practice was longer than 3 weeks. Patients who were suspected to have a diagnosis of pneumonia, based on symptoms and physical examination, were excluded.

How this fits in

In the treatment of acute exacerbations of COPD, short courses of steroids are the primary treatment. However, antibiotic treatment is in most cases not indicated. Despite wide availability of treatment guidelines, this study found that GPs prescribed antibiotics more often than indicated.

The number of patients with exacerbations, number of exacerbations per patient, daily medication, and treatment prescribed for the exacerbation were registered. Exacerbations treated by pulmonologists after having been referred by a GP were counted separately.

Statistical analysis

SPSS (version) 11.5.1 was used for statistical analysis. Differences between patients groups were analysed using χ^2 test. Statistical significance was set at $P < 0.05$.

RESULTS

Characteristics of primary healthcare centres and patients

During the 2-year study period, 35 589 patients were registered at the four primary healthcare centres. Of these patients, 458 were registered with a diagnosis of COPD (1.3%). Median age of patients with COPD was 70 years (interquartile range = 61–77 years). Daily medication for COPD was taken by 380 (84%) patients: 83 (18%) inhaled β_2 agonists and/or anticholinergics only and 297 (66%) inhaled corticosteroids, with or without β_2 agonists and/or anticholinergics. One hundred patients (22%) used N-acetylcysteine, 22 of them without inhaled corticosteroids.

A total of 572 exacerbations in 2 years were identified in 458 patients (0.62/patient/year). In 215 patients (47%) no exacerbation in 2 years occurred, 162 (35%) had one or two exacerbations, and 81 (18%) exacerbated more often (Table 1). In patients with exacerbations, there was a median of two exacerbations over 2 years (range = 1–13)

Treatment of exacerbations

Of the 572 exacerbations, 36 (6%) were treated by pulmonologists. In the remaining 536 exacerbations, GPs prescribed a short course of oral steroids in 161 cases (30%), antibiotics in 157 (29%), and steroids were combined with an antibiotic in 121 (23%). In 97 cases (18%) no steroid course or antibiotic was prescribed, but compliance to daily medication use was checked and/or this medication was adapted (Table 1).

Table 1. Characteristics of patients and treatment of exacerbations.

	n (%)
Patients	35 589
Patients with COPD	458 (1.3)
Maintenance medication ^a	
β ₂ agonists/anticholinergics	83 (18)
Inhaled corticosteroids (± β ₂ agonists/anticholinergics)	297 (66)
No daily medication used	71 (16)
Incidence of exacerbations over 2 years	
Patients with no exacerbations	215 (47)
Patients with 1 or 2 exacerbations	162 (35)
Patients with ≥3 exacerbations	81 (18)
Treatment of exacerbations (n = 572)	
Antibiotics	157 (29)
Short course of steroids	161 (30)
Antibiotics and steroids	121 (23)
No antibiotics and no steroids	97 (18)
Treated by pulmonologist	36 (6)

^aSeven patients used medication that fell outside the three medication groups. Three patients used acetylcysteine only, two were on theophylline, and maintenance medication was not known for two patients.

Treatment was influenced by patient characteristics. Compared with patients with one or two exacerbations, patients with three or more exacerbations were prescribed significantly more steroid courses and steroids combined with antibiotics, and less antibiotics without steroids or no antibiotics or steroids ($P \leq 0.001$ in all cases). In patients younger than 70 years, antibiotics without steroids were prescribed more often than in patients over 70 years of age ($P = 0.02$) (Table 2).

Steroid courses were usually prescribed in a dose of 30 mg per os daily for 7 or 10 days. The most frequently prescribed antibiotics were amoxicillin/clavulanate (co-amoxiclav) for 7 or 10 days (34%), doxycycline for 8 days (28%), amoxicillin for 7 days (18%), and azithromycin for 3 days (12%).

DISCUSSION

Summary of main findings

In this retrospective analysis of the medical records of patients with COPD in general practice, almost half of the patients had no acute exacerbation in the 2-year study period, one-third had one or two exacerbations, and one in five patients with COPD

exacerbated more often. In instances where patients had an exacerbation of COPD, GPs often did not prescribe treatment in accordance with the Dutch College of General Practitioners guidelines for COPD.¹⁰ Antibiotics were often prescribed (52% of the exacerbations), and in almost 30% an antibiotic was the only medication prescribed.

GPs in the four primary healthcare centres treated half of the exacerbations with steroid courses. Evidence from the literature indicates that short courses of steroids are beneficial in exacerbations of COPD,¹⁻³ and most international guidelines advise short courses of oral steroids for patients at home.^{12,13} However, only the GOLD guidelines (Global Initiative for Chronic Obstructive Lung Disease) include FEV1 below 50%.¹⁴ The Dutch College of General Practitioners guidelines for COPD are even more restrictive by advising short courses of oral steroids only in more severe exacerbations. In this sense, GPs appear to follow the Dutch guidelines.¹⁰

GPs in this study prescribed antibiotics in 23% of cases combined with steroids and in 29% of the cases without steroids. The Dutch guidelines for COPD is restrictive regarding when to prescribe antibiotics for exacerbations of COPD. They are more restrictive than the international standards, which mention altered sputum characteristics as an indication for antibiotics. It is unlikely that slightly more than half of all exacerbations in the current study fulfil the criteria of the Dutch guidelines for prescribing antibiotics. The prescription of antibiotics for exacerbations of COPD in daily practice will be even higher, as exacerbations with signs of pneumonia were excluded from the study. The possibility that GPs may sometimes label an exacerbation as a pneumonia to justify prescribing antibiotics cannot be excluded.

Guidelines are there to assist GPs to treat patients using an evidence-based approach and are not a protocol that always has to be followed in a strict way. As in general practice assessing the severity of an exacerbation may be difficult in some cases, GPs may prescribe antibiotics to be on the safe side. It is unclear why antibiotics were prescribed much more frequently than indicated in the Dutch guidelines. The Dutch guidelines may be too stringent to be followed

Table 2. Treatment of exacerbations: influence of patient characteristics.

	Exacerbations n (%)			Age in years n (%)		
	1 or 2 (n = 205)	3 (n = 331)	P-value ^a	70 (n = 273)	>70 (n = 263)	P-value ^a
Antibiotics	76 (37)	81 (24)	0.001	91 (33)	66 (25)	0.02
Short course of steroids	42 (20)	119 (36)	<0.001	72 (26)	89 (34)	0.09
Antibiotics and steroids	27 (13)	94 (28)	<0.001	63 (23)	58 (22)	0.67
No antibiotics/ no steroids	60 (29)	37 (11)	<0.001	47 (17)	50 (19)	0.68

^aχ².

in daily practice; for example, GPs may suspect that withholding antibiotics may lead to hospitalisation. Alternatively, deviation from the guidelines may not be clinically justified in many cases. It is unclear whether guidelines or prescribing patterns should be changed, and further study is required.

Prescriptions in patients with one or two exacerbations differed significantly from prescriptions for patients with three or more exacerbations. Short courses of oral steroids were prescribed more frequently in patients with three or more exacerbations, and antibiotics only were prescribed less frequently. Treatment in patients with three or more exacerbations was more in accordance with the Dutch guidelines than treatment in patients having one or two exacerbations.

Limitations of the study

Analysing medical records has its limitations. Because this evaluation was conducted retrospectively, information about specific symptoms during exacerbations of COPD could not be obtained. Although all patients were registered using the ICPC code for COPD, and the diagnoses of COPD made by GPs were confirmed by spirometric testing for almost all patients, it cannot be ruled out that the study might have included some patients with asthma.

Comparison with existing literature

Research published in 1998 showed that GPs prescribe antibiotics more frequently and steroid courses less frequently than indicated by the Dutch guidelines.¹⁹ Although the Dutch guidelines have been revised several times since then, little has changed in the treatment of exacerbations of COPD in primary health care. An evaluation of the most important barriers to change is indicated.²⁰

Implications for clinical practice

In the general population there is an association between antibiotic consumption and resistance to pathogens.^{15–18} Unnecessary use of antibiotics should be avoided to prevent antimicrobial resistance of pathogens. Therefore, the current authors suggest that concerted efforts should be made to fully implement the Dutch guidelines for COPD.

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Ethics committee

As the medical records of patients were retrospectively analysed, ethical approval was not applicable to the current research

Competing interests

The authors have stated that there are none.

REFERENCES

1. Aaron SD, Vandemheen KL, Hebert P, *et al.* Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease. *N Engl J Med* 2003; **348**(26): 2618–2625.
2. Davies L, Angus RM, Calverley PM. Oral corticosteroids in patients admitted to hospital with exacerbations of chronic obstructive pulmonary disease: a prospective randomised controlled trial. *Lancet* 1999; **354**(9177): 456–460.
3. Niewoehner DE, Erbland ML, Deupree RH, *et al.* Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. Department of Veterans Affairs Cooperative Study Group. *N Engl J Med* 1999; **340**(25): 1941–1947.
4. Anthonisen NR, Manfreda J, Warren CP, *et al.* Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987; **106**(2): 196–204.
5. Allegra L, Blasi F, de Bernardi B, *et al.* Antibiotic treatment and baseline severity of disease in acute exacerbations of chronic bronchitis: a re-evaluation of previously published data of a placebo-controlled randomized study. *Pulm Pharmacol Ther* 2001; **14**(2): 149–155.
6. Saint S, Bent S, Vittinghoff E, Grady D. Antibiotics in chronic obstructive pulmonary disease exacerbations. A meta-analysis. *JAMA* 1995; **273**(12): 957–960.
7. Hirschmann JV. Do bacteria cause exacerbations of COPD? *Chest* 2000; **118**(1): 193–203.
8. Jorgensen AF, Coolidge J, Pedersen PA, *et al.* Amoxicillin in treatment of acute uncomplicated exacerbations of chronic bronchitis. A double-blind, placebo-controlled multicentre study in general practice. *Scand J Prim Health Care* 1992; **10**(1): 7–11.
9. Sachs AP, Koeter GH, Groenier KH, *et al.* Changes in symptoms, peak expiratory flow, and sputum flora during treatment with antibiotics of exacerbations in patients with chronic obstructive pulmonary disease in general practice. *Thorax* 1995; **50**(7): 758–763.
10. Geijer RMM, van Schaijck CP, van Weel C, *et al.* NHG-Standaard COPD: Behandeling. *Huisarts Wet* 2001; **44**(5): 207–219.
11. WONCA (World Organization of Family Doctors Classification Committee). *ICPC-2-R: International Classification of Primary Care*, revised 2nd edn. Singapore: WONCA, 2005.
12. American Thoracic Society/European Respiratory Society Task Force. *Standards for the diagnosis and management of patients with COPD*. New York: American Thoracic Society; 2004 [updated 2005 September 8]. <http://www-test.thoracic.org/copd/> (accessed 21 Jul 2006).
13. National Collaborating Centre for Chronic Conditions. Chronic obstructive pulmonary disease. National clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004; **59**(Suppl 1): 1–232.
14. Global Initiative for Chronic Obstructive Lung Disease. *Pocket guide to COPD diagnosis, management, and prevention. A guide for health care professionals*. Global Initiative for Chronic Obstructive Lung Disease, 2005. <http://www.goldcopd.com/GuidelineItem.asp?intId=1116> (accessed 21 Jul 2006).
15. Bronzwaer SL, Cars O, Buchholz U, *et al.* A European study on the relationship between antimicrobial use and antimicrobial resistance. *Emerg Infect Dis* 2002; **8**(3): 278–282.
16. Chen DK, McGeer A, de Azavedo JC, Low DE. Decreased susceptibility of *Streptococcus pneumoniae* to fluoroquinolones in Canada. Canadian Bacterial Surveillance Network. *N Engl J Med* 1999; **341**(4): 233–239.
17. Felmingham D, Gruneberg RN. The Alexander Project 1996–1997: latest susceptibility data from this international study of bacterial pathogens from community-acquired lower respiratory tract infections. *J Antimicrob Chemother* 2000; **45**(2): 191–203.
18. Seppala H, Klaukka T, Vuopio-Varkila J, *et al.* The effect of changes in the consumption of macrolide antibiotics on erythromycin resistance in group A streptococci in Finland. Finnish Study Group for Antimicrobial Resistance. *N Engl J Med* 1997; **337**(7): 441–446.
19. Smeele IJ, Van Schayck CP, Van Den Bosch WJ, *et al.* Discrepancy tussen de richtlijnen en het handelen van huisartsen bij volwassenen met exacerbatie van astma of COPD. [Discrepancy between the guidelines and practice by family physicians in treating adults with an exacerbation of asthma or chronic obstructive pulmonary disease]. *Ned Tijdschr Geneesk* 1998; **142**(42): 2304–2308.
20. Cabana MD, Rand CS, Powe NR, *et al.* Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; **282**(15): 1458–1465.