

NOTES AND COMMENTS

Viral and atypical pathogens as causes of type 1 acute exacerbations of chronic bronchitis

Clin Microbiol Infect 1997; 3: 513–514

Considerable controversy exists regarding the role of antibiotics in managing exacerbations of chronic obstructive pulmonary disease (COPD). Both viruses and bacteria are involved in its pathogenesis. There have been many trials to determine the value of antibiotic treatment in acute exacerbations, but most can be criticized because of patient selection criteria, lack of controls, inappropriate analysis and subjective assessments [1]. One placebo-controlled landmark study by Anthonisen et al [2] showed that antibiotic therapy shortened the duration of the exacerbation and prevented deterioration, especially in the severest type 1 (worsening dyspnea, increased sputum volume and purulence) exacerbation. Moreover, a recently published meta-analysis on studies using an antibiotic in the treatment and a placebo in the control group suggested a small but statistically significant improvement due to antibiotic therapy in patients with exacerbations of COPD [3].

In an editorial in the *Lancet* [1] after Anthonisen's study it was, however, concluded that the question of the need for antibiotic treatment in exacerbations of

COPD still remained unanswered, especially because no assessment of the causative microorganisms was made and because, on clinical grounds alone, one is unable to do so [1].

In the last five years we have carried out four studies in patients with acute exacerbations of chronic bronchitis in collaboration with chest physicians in several hospitals in The Netherlands (Table 1) [4–7]. The definitions of the American Thoracic Society for chronic bronchitis were used. In all studies, only patients (357) with the severest form (type 1) of exacerbations according to Anthonisen et al were included. The mean ages of patients were between 55 and 65 years. Patients with a pneumonia were excluded from this analysis. Following collection of purulent sputum for bacterial cultures, blood samples were obtained on the first and the third visit (day 12–16) from 305 of them for serologic determination. Antibodies against respiratory pathogens such as influenza viruses A and B, parainfluenza viruses 1–4, respiratory syncytial virus, adenovirus, *Chlamydia psittaci*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila* and *Coxiella burnetii* were determined. Tests were done by a complement-fixation assay, *Chlamydia* (genus-specific enzyme immunoassay) and *L. pneumophila* (latex agglutination and enzyme immunoassay)

Table 1 Viral infections and atypical pathogens as causes of acute exacerbations of COPD

	Number of patients	Patients with viral infection	Causative viral or atypical pathogen
Rademaker et al [4]	50 ^a	3 (6%)	<i>Chlamydia pneumoniae</i> (4) <i>Mycoplasma pneumoniae</i> (1) Influenza A (2) Respiratory syncytial-virus (1)
Mertens et al [5]	50	2	<i>Legionella pneumophila</i> (1) <i>Chlamydia pneumoniae</i> (1) Influenza A (2)
Hoepelman et al [6]	71	1	<i>Legionella pneumophila</i> (1) <i>Chlamydia pneumoniae</i> (1) <i>Chlamydia</i> spp. (2) Respiratory syncytial-virus (1)
Hoepelman et al [7]	134	12	<i>Chlamydia</i> spp (2) <i>Legionella pneumophila</i> (1) Influenza A/B (6) Parainfluenza (3) Respiratory syncytial-virus (3)

^aSerology was performed in 50 patients out of 102 patients (for budget reasons).

excepted. A viral infection or an infection with one of the other pathogens was assumed in patients with at least a fourfold rise in antibody titers or an IgM response.

Overall, evidence for a viral or atypical pathogen as a cause of infection was found in 28 patients (9.2%). A viral cause was found in 18 (5.9%). Positive serology for an atypical pathogen was documented 14 times in 12 patients. Two patients had a viral and an atypical pathogen as the cause of their infection. In the largest of our studies, we could establish a correlation between eradication of the pathogen and clinical cure [7]. The rate of infection is somewhat lower than those reported in the past in unselected patients (type 1–3). It is assumed that in less severe cases (type 2/3) viruses play a more important role [3]. It is remarkably lower (over 40%) in comparison to a study by Nicholson et al [8] in younger patients (mean age 33 years) with asthma, who used new methods (polymerase chain reaction, PCR) to identify rhinoviruses and coronaviruses. A recent study by the Netherlands institute of primary health care (NIVEL) used this method to identify pathogens in influenza-like illness; in an additional 30% of patients, a pathogen could be identified (unpublished observations). We therefore conclude that the viral and atypical causes sought in our studies (excluding corona viruses and rhinoviruses) are uncommon causes of type 1 exacerbations. However, a new study of the severest form of exacerbation (type 1) using PCR as well as viral culture is needed.

Acknowledgment

Presented at the 35th ICAAC, San Francisco, abstract K 174.

Peter H. Roessingh¹, Anton M. van Loon²,
Jan W. J. Lammers³, Andy I. M. Hoepelman^{1,2}

¹University Hospital,

Department of Medicine,

Division of Infectious Diseases and AIDS,

Utrecht, The Netherlands;

²Medical Diagnostic Center for Virology; and

³Department of Respiratory Diseases,

Eijkman-Winkler Institute for

Medical Microbiology,

University Hospital,

Utrecht, The Netherlands

References

1. Editorial. Antibiotics for exacerbations of chronic bronchitis? *Lancet* 1987; 334: 23–4.
2. Anthonisen NR, Manfreda J, Warren CPW, Hershfield ES, Harding GKM, Nelson NA. Antibiotic therapy in exacerbation of chronic obstructive pulmonary disease. *Ann Intern Med* 1987; 106: 196–204.
3. Saint S, Bent S, Vitnnghoff E, Grady D, Grady D. Antibiotics in chronic obstructive pulmonary disease, a meta-analysis. *JAMA* 1995; 273: 957–60.
4. Rademaker CMA, Sips AP, Beumer HM, et al. A double-blind comparison of low-dose ofloxacin and amoxicillin/clavulanic acid in acute exacerbations of chronic bronchitis. *J Antimicrob Chemother* 1990; 26 (suppl D): 75–81.
5. Mertens JCC, van Barneveld PWC, Asin HRG, et al. Double blind randomized study comparing the efficacies and safeties of a short (3-day) course of azithromycin and a 5-day course of amoxicillin in patients with acute exacerbations of chronic bronchitis. *Antimicrob Agents Chemother* 1992; 36: 1456–9.
6. Hoepelman IM, Sips AP, van Helmond JLM, et al. A single-blind comparison of three-day azithromycin and ten-day co-amoxiclav treatment of acute lower respiratory tract infections. *J Antimicrob Chemother* 1993; 31(suppl. E): 147–52.
7. Hoepelman IM, Möllers MJ, van Schie MH et al. Azithromycin (A) tablets for 3 days versus 10 days Augmentin (AUG) in adults with lower respiratory tract infection. *Int J Antimicrob Agents* (in press).
8. Nicholson KG, Kent J, Ireland DC. Respiratory viruses and exacerbations of asthma in adults. *Br Med J* 1993; 307: 982–6.

The clinical microbiologist's contribution to audit, quality and guidelines

Clin Microbiol Infect 1997; 3: 514–517

In the UK, clinicians are obliged to take part in clinical audit, defined as the systematic critical review of the quality of medical care, including the procedures used for diagnosis and treatment, the use of resources and the resulting outcome. Pressures of cost containment and competition are intensifying the attention given to quality of care. Clinical microbiologists have an important role in the maintenance and improvement of the quality of patient care through their contributions to the diagnosis, management and prevention of infection.

Historically, much emphasis has been placed on assurance of the quality of diagnostic activities within the clinical laboratory, particularly technical expertise. There are voluntary and compulsory arrangements to assess and assure the competence of the scientific and technical procedures carried out there. Some warn that there are too many [1]. Laboratories may run parallel internal quality assurance schemes [2–4]. Periodic external review of a laboratory's proficiency is used as the basis for formal accreditation in many countries [5] but it covers only one aspect of the diagnostic cycle, albeit an important one. Accreditation and quality