Efficacy and Tolerability of Clarithromycin versus Azithromycin in the Short-Course Treatment of Acute Bronchitis

W. Vincken¹ and J.C. Yernault ²
1 Department of Pneumology, Vrije Universiteit, Brussels, Belgium
2 Université Libre de Bruxelles, Brussels, Belgium

Summary

In general practice it is common to prescribe antibiotics for patients with acute bronchitis presumed to be of bacterial origin. This phase III double-blind randomised multicentre study compared the efficacy and safety of clarithromycin 250mg twice daily administered for 5 days, and azithromycin 500mg once daily on day 1 followed by 250mg once daily on days 2 to 5, in the treatment of 214 adult patients with acute bronchitis. Clinical evaluations were performed pretreatment, on day 6 or 7, and at a follow-up visit between 20 to 30 days after the start of treatment.

Of the 214 patients enrolled in the study, 109 were in the clarithromycin group and 105 in the azithromycin group. The groups were matched for age, sex, smoking history and severity of actual disease.

Both regimens were well tolerated and effective. No significant differences were observed between the clarithromycin and azithromycin groups in post-treatment clinical cure (65%, 70 of 108; 53%, 55 of 103, respectively), in clinical success (96%, 104 of 108; 92%, 95 of 103, respectively), in relapse rates (1%, 1 of 101; 2%, 2 of 95) or in the numbers of patients reporting drug-related adverse events (12%, 13 of 109; 16%, 17 of 105, respectively).

Clarithromycin, administered for 5 days, was at least as effective and as safe as a 5-day azithromycin regimen in the treatment of acute bronchitis.

It is usual to initiate empirical antibiotic treatment for respiratory tract infection because of the practical difficulties in determining causal diagnosis, e.g. infectious or noninfectious, viral or bacterial (Pennington 1988).

Clarithromycin in a short treatment course of 5 days has been shown to be effective in treating bronchitis (Adam 1993; O'Neill et al. 1991; Vogel 1991). Azithromycin, another neomacrolide, has tissue concentrations that persist several weeks after treatment, also allowing a 5-day dosage regimen in the treatment of bronchitis (Peters et al. 1992). Clarithromycin, with its active metabolite 14 OH-clarithromycin, and azithromycin have antibacterial activity against the usual respiratory microorganisms, including Haemophilus influenzae (Verhaegen & Verbist 1992).

The aim of this study was to compare the ef-
ficacy, safety and relapse rates of clarithromycin and azithromycin in the short term treatment of patients with bronchitis.

**Materials and Methods**

This phase III double-blind randomised clinical study involved treating adult patients with acute bronchitis with either clarithromycin (Abbott Belgium, packaged by Bio-Pharma) 250mg twice daily for 5 days or azithromycin (Pfizer UK, packaged by Bio-Pharma) 500mg on day 1 followed by 250mg once daily on days 2 to 5. The protocol was approved by the ethical committee of the Université Libre de Bruxelles.

**Patients**

Patients were enrolled at 24 general practitioner sites in Belgium between 1 December 1992 and 1 April 1993. Male and female patients, aged 18 to 65 years, were enrolled in the study if they were diagnosed as having bronchitis, based on a history and physical examination. Patients were included if they presented 3 or more of the following clinical signs and symptoms: cough; sputum colour or consistency indicative of an acute bacterial infection; pyrexia; chest discomfort; development of/or increase in dyspnoea, rales or rhonchi. Patients had to be currently working and give their clear consent for participation in the study.

Patients were excluded from the study if they: had a history of asthma; had a history of sensitivity to macrolides; had been previously enrolled in this study; had required antibiotic therapy for other infectious diseases; had taken antibiotic therapy in the 15 days prior to the study; were lactating, pregnant or at risk of becoming pregnant during the course of the study.

**Methods**

On study day 1 (visit 1) a medical history was obtained that included the number of lower respiratory tract infections (LRTI) within the past 12 months (including the present infection), smoking habits, occupational history, and any underlying pulmonary or other clinically significant medical condition. The patients also underwent a physical examination that included recording weight and height and an evaluation of vital signs including body temperature, respiration rate, pulse rate and supine blood pressure.

Clinical signs and symptoms were graded for sputum as absent, mucoid, mucopurulent or purulent; for cough as absent, mild, moderate or severe; for dyspnoea as absent, mild, moderate or severe; for rales, rhonchi or cyanosis as absent or present. Fever was rated as absent if body temperature was less than 37.8°C. Infection status was assessed and classified as mild, moderate or severe, and the overall clinical condition as good, fair or poor. Sputum culture, clinical laboratory tests and chest x-ray were done at the discretion of the physician.

Patients returned to the study site between days 6 and 7 (visit 2) for assessment of clinical signs and symptoms and vital signs (as described for visit 1), clinical response to therapy, adverse events and concurrent medications.

Patients were withdrawn from the study upon request or if the investigator determined that discontinuation was in the best interest of the patient for any reason, including noncompliance or occurrence of an adverse event.

**Clinical Assessment**

Clinical response to therapy was assessed as: clinical cure (pretreatment signs and symptoms of the infection resolved), clinical failure (no improvement in pretreatment signs and symptoms), undetermined (clinical response to therapy could not be determined) or clinical relapse (visit 3 only; signs and symptoms of original infection reappeared in the follow-up period). Clinical success was defined as cure plus clinical improvement. Adverse events were rated as mild, moderate or severe, and were rated by the investigator to assess their relationship to the study drug as follows: not related, remotely related, possibly related, probably related or definitely related.