Low-dose/Long-term Erythromycin for Treatment of Bronchiolitis Obliterans Organizing Pneumonia (BOOP)

YOICHIRO ICHIKAWA, HIDEAKI NINOMIYA, MAKO KATSUKI, MARIKO HOTTA, MASAKO TANAKA AND KOTARO OIZUMI

Department of Medicine, Kurume University School of Medicine, Kurume, 830 Japan

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Summary: Bronchiolitis obliterans organizing pneumonia (BOOP) is a pathologic entity characterized by intraluminal fibrosis of distal air spaces. Corticosteroids have been widely used for the treatment of this condition, and most patients showed a dramatic response to it. However, long-term treatment with corticosteroids, which often increases the risk of several undesirable side-effects, is usually required because a relapse tends to occur soon after termination of treatment. We administered erythromycin (EM) at low-dose (600 mg daily) for 3-4 months to 6 patients with BOOP, and obtained a good clinical, radiological, and physiological improvement. This suggests that EM can be successfully used, instead of corticosteroids, in the treatment of BOOP.

Key words: bronchiolitis obliterans — organizing pneumonia — erythromycin — treatment — bronchoalveolar lavage

Introduction

Bronchiolitis obliterans organizing pneumonia (BOOP) (Epler et al. 1985) is recognized as a pathologic condition characterized by intraluminal fibrosis (polypoid proliferation of granulation tissue) of distal air spaces common to various lung injuries. Clinically, three types of BOOP may be distinguished, namely multiple patchy pneumonia, solitary pneumonia and diffuse interstitial lung disease (Cordier et al. 1989). Although this is a recently recognized entity, there had been reports of it previously (Grinblat et al. 1981; Davison et al. 1983).

Epler et al. (1985), by whom the term of BOOP, now widely accepted, was coined, emphasized that the diagnostic distinction from the spectrum of infiltrative lung diseases including idiopathic fibrosing alveolitis is important because most patients with BOOP have a favorable prognosis and response to corticosteroids. Corticosteroids (Basset et al. 1986) have been widely used for the treatment of BOOP although a few patients were reported to improve with antibiotics, or spontaneously (Epler et al. 1985). However, a short course treatment of corticosteroids for BOOP results in a relapse soon after termination of the treatment (Epler et al. 1985; Cordier et al. 1989), so usually long-term treatment, from several weeks to more than a year, is required. The long-term treatment with corticosteroid may bring about such severe undesirable effects as steroid diabetes, osteoporosis, iatrogenic Cushing syndrome, adrenocortical atrophy, spread of infection, peptic ulcer or brain excitability.
We reported recently that low-dose erythromycin (EM) administration was clinically effective without any side effects for chronic bronchiolitis patients through its antiinflammatory action but not simple antimicrobial activity (Ichikawa et al. 1992). Since bronchiolar inflammation is common to both chronic bronchiolitis and BOOP, we considered that low-dose EM may be useful for the treatment of BOOP too.

**Subjects and Methods**

In the present study, we performed low-dose/long-term EM administration in six patients with biopsy-proven BOOP. Patients were all women aged 52.0±21.8 (18-83) years. Symptoms were a persistent dry cough in 5, a dyspnea on exertion in 2, and a low grade fever in 2. Crackles were heard on chest auscultation in 5 of the patients. The chest roentgenogram and CT film showed multiple patchy pneumonia in 4 and diffuse interstitial lung disease in the remaining 2 patients. Physiologic studies showed a reduced vital capacity in 3 of the patients, as well as a reduced transfer factor for carbon monoxide in 4 patients (in the remaining 2 patients, transfer factor could not be examined because of a severe reduction of vital capacity). Initial bronchoalveolar lavage (BAL) showed lymphocytosis in 3, increase of both lymphocytes and neutrophils (mixed type) in 2, and neutrophilia in one (Table 1). Respiratory infection with bacteria, fungi, mycoplasma, legionella, and chlamydia were not confirmed in any of the patients by culture examinations and serologic tests.

**Results**

All patients received oral EM (600 mg daily), and showed only a few clinical and radiological improvement within a period of 2 to 4 weeks. Thus, the response to EM therapy was usually slowly and not as dramatic as with corticosteroids. Only one patients recovered completely in clinical condition and radiological findings with EM therapy during 2 months, but the remaining 5 patients recovered completely after 3 months of EM therapy. Physiologically, both %DLco and PaO₂ increased significantly after 3 months of treatment. Also, increased inflammatory cells in BAL fluid were reduced and abnormal BAL fluid cell population was nearly normalized in all patients. EM therapy was continued during a period of 3 to 4 months without any side effects. The patients have been relapse free for 3.6±1.8 (1 to 6) months.
**Discussion**

Etiology and pathogenesis of idiopathic BOOP remains unknown. An immunologic disorder in response to various lung injuries has been suggested (Epler et al. 1985; Cordier et al. 1989) because of the dramatic response of BOOP to corticosteroids in most cases. Most patients with BOOP did not respond to various antibiotics (Cordier et al. 1989; Bellomo et al. 1991). This resistance to antibiotics is an important clinical criterion suggesting BOOP. Usually, antibiotic treatment tends to be regarded as ineffectual if the clinical condition does not improve within several days. However, clinical improvement by EM in patients with BOOP was not induced immediately, and required usually a long-term period of treatment. Certain antibiotics including EM are known to have not only a simple bacteriocidal function but also to have effects on the immune response (Hauser and Remington 1982; Nelson et al. 1987). Our results, especially the normalization of BAL fluid cell population in BOOP patients even though infection was never confirmed, suggest that EM is effective in patients with BOOP because of an antiinflammatory action but not of a bacteriocidal effect. The successful treatment of these patients suggests that EM is a useful drug instead of corticosteroids for treatment of BOOP.

**References**


