

August 2014 Phoenix Pulmonary Journal Club: The Use of Macrolide Antibiotics in Chronic Respiratory Disease

This month's journal club reviewed the role of macrolide antibiotics in chronic respiratory disease. Macrolide usage was suggested from observational studies in Japan in diffuse panbronchitis, a disorder associated with chronic respiratory infection, usually *Pseudomonas aeruginosa* (1). Clinical improvement was noted despite doses of antibiotics well below the minimal inhibitory concentration (MIC) of the antibiotic. This suggested the antibiotic was likely working by an anti-inflammatory effect. These observations were extended to cystic fibrosis (CF) where prophylactic macrolide therapy in CF patients infected with *Pseudomonas* has become standard therapy (2). More recently, low dose macrolide therapy has been applied to non-CF lung diseases such as chronic obstructive pulmonary disease (COPD), bronchiectasis and asthma.

Time did not permit a review of all studies so a representative sample was discussed. In patients with COPD, the four randomized, placebo-controlled trials reviewed all suggested that chronic therapy with macrolide antibiotics reduced COPD exacerbations (3-5). This beneficial effect was confirmed by 2 recent meta-analysis (6,7). Similarly, three recent randomized trials in bronchiectasis demonstrated a reduction in exacerbations (8-10). In asthma the data is not as clear. A recent trial did not demonstrate an overall reduction in asthma exacerbations or lower respiratory tract infections (11). However, in the patients with non-eosinophilic, predominantly neutrophilic, asthma there was a reduction. An excellent review of the use of macrolides in acute and chronic asthma was recently published. (12). The article includes a review of the anti-inflammatory and immunomodulatory properties of the macrolides.

The respiratory disorders where macrolides have been shown to have clinic benefit such as diffuse panbronchitis, cystic fibrosis, COPD, bronchiectasis and non-eosinophilic asthma are all diseases associated an influx of neutrophils into the airways. The beneficial clinic effects of macrolides are consistent with their effect in reducing neutrophil chemotactic factors such as interleukin (IL)-8 (13). However, macrolides have also been reported to have adverse clinical effects such as QT prolongation in patients with heart disease, impaired hearing and development of bacterial resistance (4,6,14). Whether all COPD patients should be treated with macrolides is controversial but most in the audience used these in patients with frequent exacerbations. It was also pointed out that other antibiotics such as the tetracyclines also have anti-inflammatory effects and have been shown to be efficacious in some respiratory diseases (15). Whether the tetracyclines are equally or more effective than the macrolides with fewer serious side effects is unknown.

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