Clarithromycin and Prednisolone Inhibit Cytokine Production in Chronic Rhinosinusitis

Laryngoscope 112: Oct 2002 1827-1830

Griffith University and Princess Alexandra Hospital, Brisbane, Australia

Ri 張繼中/VS許巍鐘
Introduction

- Administration of macrolide is effective in treatment of chronic rhinosinusitis.
  ~Hashiba M et al. / Kikuchi S. et al.

- Corticosteroids are present the drug of choice in the treatment of chronic airway inflammation.
Introduction

- Hypothesis: Macrolides are able to reduce cytokine production by chronic rhinosinusitis mucosa.

- Used cultures of whole sections of patient’s sinus mucosa.
Methods

- Sinus mucosal specimens were obtained from 11 patients (6 men and 5 women, age 27~62, median 48 y/o) undergoing functional endoscopic sinus surgery.

- The diagnosis was made on the basis of symptoms and signs present for a minimum of 8 weeks in the presence of abnormalities on computed tomography (CT) scan.
Methods

- 2 patients had history of asthma; 5 patients have positive findings on allergy skin-prick tests.

- Patients who took antibiotics or corticosteroids in the 2 weeks before surgery and who have gross nasal polyposis were excluded.
Methods

- Specimen→9 pieces, placed in cultured medium.

- Clarithromycin/prednisolone was added in serial concentrations.

- After 24 hours→cell viability test→Complete Protease Inhibitor Cocktail, centrifuged.
Methods

- The concentration of IL-5, IL-8 and GM-CSF were measured using ELISA.

- ANOVA / Wilcoxon signed rank test.
Results

- The concentration-dependent reduction in IL-5, IL-8 and GM-CSF production by specimens cultured in the presence of clarithromycin was significant.

- Prednisolone also showed a significant concentration effect on reduction of IL-5, IL-8 and GM-CSF.
Fig. 1. Interleukin-5 production in the presence of clarithromycin and prednisolone compared with control specimens. A statistically significant, linear concentration-dependent reduction was seen with clarithromycin ($P<.039$) and prednisolone ($P<.013$). (The y-axis denotes cytokine levels expressed as picograms per milligram total protein.)
Clarithromycin maximum effect concentration ($10^{-5}$)

Prednisolone maximum effect concentration ($10^{-4}$)

Fig. 3. Granulocyte-macrophage colony-stimulating factor (GM-CSF) production in the presence of clarithromycin and prednisolone compared with control specimens. A statistically significant, linear concentration-dependent reduction was seen with clarithromycin ($P < .017$) and prednisolone ($P < .024$). (The y-axis denotes cytokine levels expressed as picograms per milligram total protein.)
Comparison of Clarithromycin and Prednisolone

- Wilcoxon signed rank test

  No significant differences were noted between the two treatment groups for any of the cytokines tested.
Discussion

- Macrolides have previously been shown to inhibit cytokine production in various cell types.

- IL-5 and GM-CSF was shown to be significantly reduced in nasal polyp tissue after treatment with corticosteroids.
Conclusion

- The present study has provided further evidence that macrolide antibiotics are capable of inhibiting cytokine production.

- Efficacy comparable to the well-established anti-inflammatory agent prednisolone.