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Title: Clarithromycin inhibits pandemic A/H1N1/2009 influenza virus infection in human airway epithelial cells

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Body: Rationale: We reported previously that clarithromycin (CAM), a macrolide antibiotic, inhibits seasonal type A influenza virus (H3N2) infection in human airways. However, the effects of CAM on infection by the pandemic A/H1N1/2009 influenza virus (A/H1 2009 pdm) have not been studied. Methods: Human tracheal epithelial cells (n=3) were pretreated with CAM (10 μM) and then infected with the A/H1 2009 pdm in 24-well plates. Results: The viral titer and the amount of interleukin (IL)-6, a pro-inflammatory cytokine, in the supernatant increased with time after A/H1 2009 pdm infection. CAM reduced the viral titer (6.7 ± 0.4 log $TCID_{50}$ units/ml/24 h for virus alone vs. 4.9 ± 0.2 log $TCID_{50}$ units/ml/24 h for virus plus CAM; $p<0.05$, mean ± SE) and IL-6 (211 ± 8 pg/ml/24 h for virus alone vs. 149 ± 7 pg/ml/24 h for virus plus CAM; $p<0.05$) 3 days after infection. CAM also reduced the number of epithelial cells detached from culture vessels 7 days after infection (32 ± 2 x 10^3/well in virus alone vs. 12 ± 2 x 10^3/well in virus plus CAM; $p<0.05$). In addition, we compared the viral titer and the numbers of detached cells after infection between the A/H1 2009 pdm and the A/H3N2 virus. The viral titer and the number of the detached cells after infection with the A/H1 2009 pdm were higher than those after infection with the A/H3N2 virus (4.1 ± 0.4 log $TCID_{50}$ units/ml/24 h and 5 ± 1 x 10^3/well for the A/H3N2 virus; $p<0.05$). Conclusion: Clarithromycin may inhibit A/H1 2009 pdm infection and may modulate airway inflammation and epithelial damage during the infection. The A/H1 2009 pdm may release higher levels of virus and may be more cytotoxic than seasonal influenza virus (H3N2).