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Enhancement of the bactericidal activity of antibiotics in hypoxic biofilms as seen in patients with chronic pulmonary disease

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Abstract

Pseudomonas aeruginosa lung infection is among the most severe complication in patients with chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF). CF related pulmonary infection is characterized by antibiotic-tolerant biofilms in the endobronchial mucus with zones of oxygen (O2) depletion mainly due to polymorphonuclear leukocyte (PMN) activity. Despite anoxic conditions, the flexible metabolism of P. aeruginosa growing in biofilms allows this pathogen to obtain energy for growth by denitrification as demonstrated by production of nitrous oxide in CF sputum samples. While the exact mechanisms affecting antibiotic effectiveness on biofilms remain unclear, accumulating evidence suggests that the efficiency of several bactericidal antibiotics such as ciprofloxacin is enhanced by stimulation of the aerobic respiration of pathogens and that lack of O2 increases their tolerance. Understanding the clinical effects of antimicrobials on biofilm development is important to avoid the use of inappropriate drugs in the event of biofilm infection. This article reviews current information about the growth of bacteria within the biofilm and the inhibitory or inducing effect of antimicrobials common in their formation by P. aeruginosa.

The effect of antibiotics used to treat biofilms of other bacteria, such as Staphylococcus aureus or Escherichia coli, has also been briefly discussed.

Reoxygenation of O2- depleted biofilms may thus improve susceptibility to ciprofloxacin possibly by restoring aerobic respiration. Such strategy was then tested using re-oxygenation of O2- depleted P. aeruginosa strain PAO1 agarose embedded biofilms by hyperbaric O2 treatment (HBOT) enhancing the diffusive supply for aerobic respiration during ciprofloxacin treatment. The demonstration of enhanced bactericidal activity of ciprofloxacin in P. aeruginosa biofilm during re-oxygenation by hyperbaric O2 treatment (HBOT) is indeed a proof-of-principle study that may translate into improved treatment of both CF and COPD patients.

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