Cystic Fibrosis Research News

Title:

Hyperbaric oxygen treatment increases killing of aggregating *Pseudomonas aeruginosa* isolates from cystic fibrosis patients

Authors:

Møller, Signe Agnete[1,2], Jensen, Peter Østrup[1,2,3], Høiby, Niels[1,2], Ciofu, Oana[2], Kragh, Kasper Nørskov[1,2], Bjarnsholt, Thomas[1,2], Kolpen, Mette[1,2]

Affiliations:

[1]Department of Clinical Microbiology, Rigshospitalet, 2100 Copenhagen, Denmark
[2]Costerton Biofilm Center, Department of Immunology and Microbiology, Faculty of Health Sciences University of Copenhagen, 2200 Copenhagen, Denmark
[3]Institute for Inflammation Research, Center for Rheumatology and Spine Diseases Rigshospitalet, Copenhagen, Denmark

What was your research question?

We asked if treatment with additional oxygen will cause aggregating (clumps of) infectious bacteria to stop being resistant to antibiotics. To mimic the lung mucus in people with cystic fibrosis (CF) in the laboratory we grew cultures of *Pseudomonas aeruginosa* (obtained from people with CF) without oxygen before adding oxygen to test whether this could re-sensitize *P. aeruginosa* to treatment with tobramycin (an antibiotic).

Why is this important?

In people with CF, chronic lung infection with *P. aeruginosa* is characterized by persistent clumps of bacteria growing in the lung mucus which have a high tolerance to antibiotics and the body's own response. The persistence cannot be explained by traditional resistance mechanisms, by tobramycin not penetrating the bacteria enough or by current susceptibility testing. However, the persistence may to some extent be explained by the fact that bacteria, which have reduced metabolic activity (chemical reactions) due to a restricted supply of oxygen, develop a tolerance to antibiotics. Persistence caused by this metabolic inactivity can therefore be part of the problem of antimicrobial resistance, that threatens people with CF with chronic lung infection.

European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

What did you do?

The isolates which we used in this study were taken from people with CF in whom *P. aeruginosa* was established to different degrees: intermittently colonized, early chronic infection and late chronic infection. *P. aeruginosa* isolates from people with CF who are intermittently colonized resemble environmental *P. aeruginosa* strains, which have a large metabolic changeability. We enabled the bacterial isolates to develop antimicrobial resistance by aggregating (clumping) in a setup that mimicked the environmental conditions in the lung mucus lacking oxygen. The tolerant bacterial aggregates were then re-sensitized to antibiotics by combining oxygen under hyperbaric pressure together with tobramycin.

What did you find?

We saw that tobramycin was more successful at killing clumps of *P. aeruginosa* formed by CF isolates when treated with hyperbaric oxygen (where oxygen is at a higher pressure that in room air). Another important finding is the ability of additional hyperbaric oxygen treatment to achieve clinically relevant bacterial killing with lower concentrations of tobramycin. This indicates that *P. aeruginosa* clumps formed by CF isolates in the lung mucus of people with CF can be treated with less tobramycin. This may be explained by the fact that hyperbaric oxygen treatment makes the bacteria switch from slow growth to fast growth which is associated with increased susceptibility to antibiotics.

What does this mean and reasons for caution?

This study has provided laboratory evidence that tobramycin treatment combined with hyperbaric oxygen treatment is more effective on *P. aeruginosa* taken from people with CF with various degrees of infection status. However, caution should be taken when selecting individuals to receive additional hyperbaric oxygen treatment as several lung disorders are considered unsuitable for this treatment.

What's next?

More studies are, however, needed to investigate how hyperbaric oxygen treatment as an addition to other combinations of antibiotics affects infectious bacteria growing in conditions resembling infected CF lungs. In addition, we need to examine the ability of additional reoxygenation with normobaric oxygen treatment (at normal atmospheric pressure) to enhance the killing of bacteria. This could pave the way for using supplemental oxygen treatment at atmospheric pressure to the treatment of lung infections in CF without the risk of barotrauma (injury caused by increased air pressure).

Cystic Fibrosis Research News

Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=Hyperbaric+oxygen+treatment+increases+killing+of+aggregating+Pseudomonas+aeruginosa+isolates+from+cystic+fibrosis+patients

cfresearchnews@gmail.com