Antibiotics for pulmonary exacerbations

Antibiotic treatment for stenotrophomonas maltophilia in people with cystic fibrosis

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Background

Stenotrophomonas maltophilia (SM) is one of the most common emerging gram – negative micro-organisms found in the sputum colture of people with cystic fibrosis and its prevalence is increasing (Hatziagorou E, 2019).

One relevant problem is that SM is a bacteria which is resistant to several antibiotics. A recent review describes the role of this opportunistic pathogen that can cause nosocomial and community-acquired respiratory and bloodstream infections and various other infections in humans (Brooke JS, 2021).

Papers from US registry studied the epidemiology of SM in CF, pointing out the association of SM with more severe and more advanced disease, but it did not appear to be a risk factor neither for earlier death nor for decline of pulmonary function. A recent cohort study from Canada showed that chronic SM infection is associated with an almost three-fold increased risk of death or lung transplantation in CF patients, but it is still unclear, however, whether chronic SM infection is simply a marker of severity of disease and ultimate mortality or it is causally related to disease progression (Waters V, 2013). The same authors studied whether SM infection follows the same pattern and shares similar risk factors for acquisition as described for Pseudomonas aeruginosa (Stanojevic S, 2013). Recently, a single center experience reported that acquisition of SM in CF was associated with an acceleration in lung function decline. Among those with chronic colonization, acquisition was also associated with increased hospitalization rates (Barsky EE, 2017). On the other side, recent results form France show the decrease in prevalence and bacterial density of lung colonisation for most of the CF pathogens, including Achromobacter spp, **Stenotrophomonas maltophilia** concomitantly to the clinical improvement, after initiation of treatment with Elexacaftor/Tezacaftor/Ivacaftor. Further studies are needed to better understand the underlying mechanisms of these microbiological changes (Mianowski L, 2024).

Chronic infection with SM has recently been shown to be an independent predictor of pulmonary exacerbation requiring hospitalization and antibiotics. However, the role of antibiotic treatment of SM infection in people with cystic fibrosis is still unclear. The role of SM as a pathogen in CF was recently reviewed by Hansen (Hansen CR, 2012) and by Parkins (Parkins MD, 2015).

Papers examining data from US (Binder AM, 2013) and EU (Viviani L, 2016) registries showed that colonization by SM is associated with a higher risk of Nontuberculous Mycobacterial infections. Finally, data from Germany and Austria showed that co-infection by SM is an independent risk factor for worse lung function in subjects with CF chronically infected by Staphylococcus aureus (Junge S, 2016).

SM is common in the sputum of people with cystic fibrosis related diabetes (CFRD), raising the question as to whether this is a risk factor for its acquisition. UK researchers investigated this issue at a population level, by using data from the UK registry. They concluded that although SM is more common in people with CFRD, it is not an independent risk-factor for SM acquisition. (Frost K, 2019) Also data from the EU CF registry confirm the relationship between CFRD and colonization by SM (Olesen HV, 2019)

A review gathers all the current knowledge on the major pathophysiological traits, their supporting mechanisms, regulation and evolutionary modifications involved in colonization, virulence, and competitive interactions with other members of the lung microbiota for this emerging pathogen, with all these mechanisms being major drivers of persistence in the CF lung (Menetrey Q, 2021).

A further recent systematic review summarized the current knowledge of the clinical impact of SM in patients with CF (Terlizzi V, 2023).

Issues

To assess the effectiveness of antibiotic treatment for SM in people with cystic fibrosis in relation to:

1. lung function and pulmonary exacerbations;
2. the eradication of SM

What is known

One CDSR (Amin R, 2020) assessed the effectiveness of antibiotic treatment for *Stenotrophomonas maltophilia* in people with CF. The authors' conclude that this review did not identify any evidence regarding the effectiveness of antibiotic treatment for *Stenotrophomonas maltophilia* in people with CF. For this reason, clinicians need to use their clinical judgement as to whether or not to treat *Stenotrophomonas maltophilia* infection in people with CF.

Randomized clinical trials are needed to address these unanswered clinical questions.

Unresolved questions

Randomized clinical trials are needed to address either microbiological (bacterial density, eradication) or clinical outcomes about SM infection in CF.

The optimal management of CF patients with persistent S. maltophilia infection is not yet known and requires further studies.

No RCT is currently ongoing on this topic.

Keywords

Bacterial Infections; Infection; Pneumonia; Respiratory Tract Infections; Stenotrophomonas Maltophilia; Anti-Bacterial Agents; Carbapenems; Cephalosporins; Monobactams; Others anti-bacterial agents; Penicillins; Quinolones; Tetracyclines;