ADHERENCE TO INHALED ANTIBIOTICS FOR THE TREATMENT OF CHRONIC PSEUDOMONAS AERUGINOSA INFECTION IN PATIENTS WITH CYSTIC FIBROSIS: A SYSTEMATIC LITERATURE REVIEW

Tamás Ágh1, Réka Bodnár2, Máté Oláh3, Ágnes Mészáros3

1. Syreon Research Institute, Budapest, Hungary; tamas.agh@syreon.eu
2. Department of Pediatric Pulmonology, Heim Pál Children's Hospital, Budapest, Hungary
3. University Pharmacy Department of Pharmacy Administration, Semmelweis University, Budapest, Hungary

Background

• Cystic Fibrosis (CF) is an inherited disease which affects particularly the lungs, pancreas, hepatobiliary system, reproductive tract and sweat glands.1
• CF is caused by mutations in the gene encoding the CF Transmembrane Conductance Regulator protein.2
• Chronic Pseudomonas Aeruginosa (PA) lung infection is the most prevalent infection of CF patients.2
• Chronic infection with PA impacts the progress of lung disease which determines the life expectancy in CF.3
• In the management of lung infection with PA, inhaled antibiotic (AB) therapy is recommended as maintenance therapy.3
• In CF medication non-adherence poses a significant barrier to optimal disease management.4

Objective

To perform a systematic literature review of adherence to inhaled antibiotics for the treatment of chronic PA infection in patients with CF.

Methods

• A systematic literature search of English-language articles was conducted in April 2015 using Medline and Embase (via Scopus).
• A combination of the following search terms were used: adheren*, persisten*, complian*, cystic fibrosis, mucoviscidosis, pseudomonas aeruginosa, antibiotic*.5
• No publication date limit was applied.
• The literature screening was conducted by 2 independent reviewers.

All of the included studies were assessed for quality using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.5

Results

Ten studies1-14 were identified and included in the systematic review (Figure 1).

The general characteristics, measurement methods and adherence results of the included studies are summarized in Table 1.

• Proportion of adherent patients:
  • randomized clinical trials: 86.4-97.3%6,7
  • real-world studies: 7-29.6%12,15
• In the included studies adherence to inhaled ABs did not differ significantly from adherence rates to other CF-related medications.10,11

Adherence to inhaled ABs was found to be associated with the complexity of treatment, time of drug administration, age of patients, treatment burden (i.e., adverse events, and taste) and patient satisfaction.

The included studies fulfilled the STROBE criteria between 52%12 and 78%13,15.

Limitations

Only studies that were published in English and indexed in the selected databases were involved in the review.

Table 1. General characteristics and adherence to inhaled antibiotic results of the included studies

<table>
<thead>
<tr>
<th>Study length</th>
<th>Subjects, total (inhaled ABs)</th>
<th>Adherence</th>
<th>Inhaled ABs</th>
<th>Measurement</th>
<th>Adherence</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 weeks</td>
<td>572</td>
<td>100%</td>
<td>Tobramycin</td>
<td>Self-report adherence</td>
<td>90%</td>
<td>32% to 86%</td>
</tr>
<tr>
<td>26 weeks</td>
<td>528</td>
<td>95%</td>
<td>Tobramycin</td>
<td>Pharmacy refill record</td>
<td>65%</td>
<td>25% to 50%</td>
</tr>
</tbody>
</table>

Conclusions

• Adherence varied depending on the type of study, type of treatment, and method of measurement.

In real-world studies poor adherence to inhaled ABs was found in patients with CF, in contrast to randomized clinical trials.

• Regular routine adherence monitoring during CF care, discussion about sub-optimal adherence and treatment reinforcement on the basis of treatment burden, clinical status, and adverse events may help to better understand the predictors and the long-term consequences of non-adherence to inhaled ABs for the treatment of chronic PA infection in CF.

Figure 1. The flow diagram of the systematic literature review process