Early treatment with inhaled antibiotics postpones recurrence of Achromobacter species in cystic fibrosis

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Objectives: In this nationwide retrospective study, we analysed early acquisition of Achromobacter spp. in Danish cystic fibrosis (CF) patients from 2000 to 2011, excluding cross-infections.

Methods: Thirty-four primary isolates were identified by partial sequencing of recA, tyrB and icd, and were subjected to extended antimicrobial susceptibility testing. Achromobacter xylosi regarding novel and innocuous therapies to combat cystic fibrosis relevant infections.

Conclusion: Our findings suggest that early treatment with inhaled antibiotics may prevent or postpone chronic infection with Achromobacter species in CF patients.

Aztreonam lysine for inhalation as a treatment for Burkholderia cepacia complex in CF

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Objectives: Aztreonam lysine for inhalation (AZLI) has been proven effective in the treatment of chronic Ps. aeruginosa (PA) infection in CF. It is not clear whether patients with other infecting organisms, such as B. cepacia complex (Bcc), could benefit from this treatment. We aim to investigate the clinical efficacy of AZLI for Bcc in CF.

Methods: We reviewed medical files of 4 patients infected with B. multivorans who were treated with AZLI. Bcc prevalence in Belgium is 2%.

Results: The patients were 26 (A, male, severe liver disease and portal hyperten- sion), 33 (B female), 14 (C, female, CFRD) and 12 (D, male) years old. A was infected for several years, whereas B, C and D were newly acquired colonisations. A and B had co-infection with PA. A, B and C were treated for 48 weeks with AZLI (28 day on/off cycle) as add-on therapy to another cyclical inhaled antibiotic, D for 12 weeks continuously as mono-inhaled therapy. In addition, A received 3-monthly courses of IV antibiotics. B, C and D had 1 IV course at time of acquisition. Mean lung function values remained stable for 48 weeks during AZLI. D showed a slight improvement in FEV1 of 4% after 12 weeks. A did not deteriorate further. In B and D, Bcc was not found in the respiratory cultures during AZLI inhalation. However in D, Bcc reappeared after AZLI was stopped. B and C had less pulmonary exacerbations after start of AZLI. No adverse effects were seen.

Conclusion: These Bcc-infected patients seem to benefit from a treatment with AZLI. In 2 recent acquisitions, eradication of B. multivorans was seen. AZLI was well tolerated, also in young patients. Clinical trials studying the efficacy of AZLI for Bcc are ongoing.

Ceftazidime continuous IV infusion in patients with cystic fibrosis and pyridine production

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Objectives: Ceftazidime (CAZ) remains one of the main anti-infective agents against P. aeruginosa in cystic fibrosis patients. Caregivers reported various disturbing phenomena of intolerance, especially in case of prolonged infusion. A spontaneous production of pyridine (P), which is a toxic product, raises some concern. Our aim was to study the kinetics of spontaneous degradation of CAZ shaped in Portable Infusion Pumps (PIPs) and the potential risk of exposure to P.

Methods: 18 PIPs LV/10 Baxter® were filled by 12g of CAZ diluted in 230 mL of saline solution. Devices were stored either at 4, 22, or 33ºC. Samples were collected immediately before and then every 4h after the shaping of PIPs until the 24h. Both CAZ and P were analysed by HPLC. Model-independent kinetic parameters were determined for both CAZ and P (Table 1). Results: See Table 1.

Table 1.

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAZ</th>
<th>Pyridine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAZ</td>
<td>Pyridine</td>
</tr>
<tr>
<td></td>
<td>4ºC (n=6)</td>
<td>22ºC (n=6)</td>
</tr>
<tr>
<td>Mean concentration (mg/mL)</td>
<td>51.7±2.5</td>
<td>0.15±0.006</td>
</tr>
<tr>
<td>Remaining volume after 24h (mL)</td>
<td>80.3±7.1</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Total delivered amount</td>
<td>7.5±1.0</td>
<td>15.6±1.0</td>
</tr>
</tbody>
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The flow controller of the devices was maintained at 37ºC.

Conclusions: Taking into account the unavoidable presence of P in the medium, we suggest:

a. to avoid exposing a solution of CAZ to over 22ºC, especially in cases of prolonged infusion,
b. to replace the once daily administration schedule by a twice daily infusion: 6g/12hrs leads to a theoretical production of 36mg (vs. 56mg) of P per day of treatment at 22ºC.

Other options to be tested are a decrease of the daily dose of CAZ and maintaining PIPs at 4ºC.