the time of illness presentation. The first-line treatment for this infection, cotrimoxazole, is associated with a number of adverse effects, including rash, leucopenia, thrombocytopenia and interstitial nephritis. Therefore, treatment with cotrimoxazole significantly adds to the morbidity associated with this condition and we note in this study that this was the main treatment used.

One of the identifying characteristics of P. jirovecii is the presence of (1,3)-β-D-glucan in its cell wall. As the cell wall of this organism does not contain ergosterol (the target of azoles and polyenes), echinocandins, which target the synthesis of (1,3)-β-D-glucan, are likely to be the only effective antifungals for PCP.

Caspofungin was the first echinocandin licensed for empirical antifungal treatment in candidiasis and aspergillosis. In animal models of PCP, echinocandins have demonstrated prophylactic and therapeutic efficacy. Furthermore, there are reports that caspofungin is effective salvage treatment for PCP. Echinocandins are associated with a low incidence of adverse events. Caspofungin does not inhibit the CYP system and does not induce CYP3A4 drug metabolism. We present our experience of the use of caspofungin in the context of severe PCP in HIV-infected individuals.

We performed a retrospective analysis of all patients treated for proven or probable PCP pneumonia over a 4 year period from our unit, the largest HIV cohort in Europe; appropriate ethical approval was obtained. For all patients, baseline demographics, CD4 count measured 109 (4-213) cells/ml; nine patients (8.8%) had microbiologically confirmed PCP by immunofluorescence. The mean CD4 count measured 109 (4-676) cells/ml; nine patients (8.8%) had microbiologically confirmed PCP with a CD4 count of >200, and a further nine had confirmed PCP with an undetectable viral load while receiving highly active antiretroviral treatment (HAART). A total of six patients had been receiving PCP prophylaxis at diagnosis. Overall mortality was 6.25% (5/85) and 5.3% (5/96) for microbiologically confirmed PCP. Five patients died overall (3 from respiratory failure, 1 from persistent pneumothorax and 1 refused all treatment).

Of these patients, 67 received cotrimoxazole as first-line treatment, six with clindamycin/primaquine, six with atovaquone, and one patient received intravenous pentamidine. Twelve individuals required a treatment switch due to cotrimoxazole-related toxicities (7 rash, 2 hepatitis, 1 hypernatraemia, 1 diarrhoea and 1 nausea). A total of 12 patients with PCP not responding to first-line treatment received caspofungin in combination with other treatments. Of these patients, 10 had microbiologically confirmed PCP. None of these patients had other relevant fungi such as Candida or Aspergillus isolated by induced sputum or bronchoalveolar lavage.

Of these 12 patients, 10 individuals received treatment with caspofungin as a component of salvage therapy after first-line treatment failure, and two received caspofungin following first-line drug toxicity. Patients received caspofungin in combination with clindamycin/primaquine (6/12), clindamycin (4/12) or intravenous pentamidine (2/12).

For the 10 patients who received caspofungin as a part of salvage therapy, two died, one from bilateral pneumothoraces which had been present since day 2 of diagnosis and one from Burkitt lymphoma. The patient with Burkitt lymphoma did not have microbiological confirmation of PCP. Therefore, for patients with microbiologically confirmed PCP treated with caspofungin, mortality was 1 in 10 or 10%.

Despite the advent of HAART for the treatment of HIV infection, PCP remains a major cause of mortality even in resource-rich settings. Recent data suggest that in the HAART era, mortality from this infection when microbiologically confirmed is ~10%. Over the last 4 years we have used caspofungin as an adjunctive treatment for the management of severe or refractory cases of PCP. Caspofungin targets the synthesis of β-glucan, a major component of the P. jirovecii cell wall. Furthermore this drug has minimal side effects and drug interactions, allowing its use as adjunctive treatment.

This single cohort study suggests that caspofungin may improve outcomes from PCP with favourable comparative mortalities in our cohort (5.3%) compared with a recent study (9.7%) of confirmed cases of PCP from a similar cohort of UK patients in the HAART era. Randomised controlled studies of caspofungin for PCP are warranted and further suggest that the prediction rule may require modification in the setting of newer treatments.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Riverside Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 4 May 2010
Published Online First 29 September 2010

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Survey of the use of non-invasive positive pressure ventilation in UK and Australasian children with cystic fibrosis

Non-invasive positive pressure ventilation (NIPPV) for respiratory failure in cystic fibrosis (CF) is frequently used in adults and has been shown to be of benefit to patients with advanced disease in terms of stabilisation of lung function, reduction in symptoms and increased exercise capacity. When used as an adjunct to physiotherapy, NIPPV increases oxygen saturations (SpO2), tidal volume, maximum expiratory muscle strength and ease of sputum clearance. Thorax June 2011 Vol 66 No 6 538

Thorax: first published as 10.1136/thx.2010.139063 on 3 September 2010. Downloaded from http://thorax.bmj.com/ on October 21, 2023 by guest. Protected by copyright.
Frequent desaturations
Baseline SaO2 <93%
SpO2 <90% for >10 sleep study
SpO2 <92% for >5% sleep study

<table>
<thead>
<tr>
<th>Hypoxia</th>
<th>Hypercapnia</th>
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<tr>
<td>PetCO2 &gt;6.7 kPa</td>
<td>CO2 &gt;6.7 kPa for &gt;25% sleep study</td>
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<tr>
<td>TCO2 rise to 6.7 kPa or rise by 0.9 kPa during sleep</td>
<td>CO2 &gt;7 kPa</td>
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CO2, carbon dioxide; PetCO2, end tidal carbon dioxide pressure; SaO2, arterial oxygen saturations; SpO2, non-invasive oxygen saturations; TCO2, transcutaneous carbon dioxide pressure.

There are no guidelines for the assessment of gas exchange or timing and mode of NIPPV initiation in patients with CF. The British Thoracic Society guideline states there is insufficient evidence to recommend its routine use in patients with CF.5 The aim of this study was to establish current practice with regard to investigation of respiratory failure, factors leading to NIPPV initiation and extent of the use of this modality across UK and Australasian (ANZ) paediatric CF centres.

A semi-structured questionnaire consisting of 21 closed and open-ended questions was sent to the lead CF consultant and CF physiotherapists of specialist paediatric CF centres in the UK (n=27) and ANZ (n=14). The response rate was 88% (25 UK centres, 11 ANZ centres), representing a total of 5954 children. Twenty-three children (0.39%) from 13 centres were using NIPPV (11 UK and 12 ANZ). The median (range) age of NIPPV initiation was 14 (6–17) years and the median (range) usage of NIPPV per night was 8 (3–10) h. Eleven of the 36 centres (31%) reported that they have a protocol for NIPPV initiation, but it was unclear whether this was specific for CF. The preferred mode of NIPPV was bi-level NIPPV (75%), followed by single-level preset pressure ventilation (19%), volume control single-level ventilation (5%) and continuous positive airways pressure (5%). Nasal masks were the most frequently used interface (47%), followed by full face masks (38%), mouthpieces (13%) and nasal pillows (2%).

Less than half of the CF centres (17/36) undertook CF sleep studies. SpO2 monitoring alone was most commonly used (51% of centres), followed by SpO2 and transcutaneous carbon dioxide monitoring (22%). Full polysomnography was less frequently used as a first-line investigation (16.2%). Assessment of respiratory failure differed between childhood CF centres, with different definitions for hypoxia and hypercapnia in use (table 1).

The principal reasons for initiating NIPPV included in an acute exacerbation, as a bridge to transplant and as an adjunct to physiotherapy. There were 19 reported NIPPV failures in children with CF from 10 centres. Reasons for failure included claustrophobia, inability to tolerate pressure, discomfort, poor initial set-up, parent or patient anxiety and poor adherence. Four adverse events were reported (issues with mask fitting and pressure sores, n=2; retained secretions, n=1; and pneumothorax, n=1).

NIPPV is rarely used in UK and ANZ paediatric CF populations, probably due to improved patient outcomes and the very low prevalence of respiratory failure in childhood CF. Bi-level NIPPV is the preferred mode of ventilation. However, there is no agreed definition of hypoxia and hypercapnia, no uniformity in assessing gas exchange and no standard protocol for the indications and institution of NIPPV in children with CF. As very few of the expected benefits of NIPPV have been proven, particularly in the paediatric CF population, and as there is a high frequency of NIPPV failure, the need for future research in this area is highlighted, beginning with the need for protocols to be developed and evaluated.

Acknowledgements The authors acknowledge Dr Michelle Chatwin and Dr Ian Balfour-Lynn, Royal Brompton Hospital, London, UK; N Collins,1 A Gupta,2 S Wright,3 L Gauld,3,4 D Urquhart,1,2,4 A Bush2

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Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 19 May 2010
Published Online First 3 September 2010

doi:10.1136/thx.2010.139063

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Effects of omalizumab in Aspergillus-associated airway disease

The clinical spectrum of Aspergillus-associated airway diseases (AAAD) includes Aspergillus-induced asthma, allergic bronchopulmonary aspergillosis (ABPA) and bronchoceptric granulomatosis. Corticosteroids are almost always used to suppress the immunological response to the fungal antigens.4 Although there are no evidence-based alternative treatment options besides steroids, the well-known adverse effects of these drugs have prompted clinicians to look beyond this standard practice and several cases of ABPA patients with very positive outcomes after omalizumab therapy have been recently published.5–6

We recruited 18 patients (13 women; mean age 49±17 years) with AAAD (2 of them had been previously diagnosed with cystic fibrosis) from 11 Spanish hospitals. All of them had been treated with omalizumab for at least 16 weeks and they were receiving inhaled corticosteroids (daily dose 1351±554 μg budesonide or its equivalent) and a long-acting β2 agonist at the moment of omalizumab initiation. Seventeen patients were being treated with oral corticosteroids at a median daily dose of 16 mg prednisone or its equivalent (IQR 6–30) and 10 with itraconazole. The mean number of albuterol puffs per day was 3.5 (range 1–8). Prior to omalizumab administration, IGE levels were (median [IQR]) 698 IU/ml (478–977) and the median absolute count of eosinophils in blood was 610 mm3 (317–1015). Sixteen of the 18 patients had CT-diagnosed bronchiectasis and fleeting pulmonary opacities were identified in 10 of them. All patients showed a delayed positive skin test for Aspergillus and 17 also developed an immediate response. Serum Aspergillus-specific IGE was found in all patients and precipitating antibodies in serum were observed in 10.

Omalizumab-treated patients were followed up for a median of 36 weeks (IQR, 28–42). The mean dose of omalizumab per week was 608±108 mg. No significant adverse effects were observed. The treatment was discontinued in five patients due to a lack of response and in another patient because of a positive test for pregnancy. The clinical and functional effects of omalizumab are summarised in table 1.

In this series, the largest reported to date, omalizumab has demonstrated a beneficial effect in reducing symptoms and exacerbations in a group of patients with AAAD. It