LETTERS

Mepolizumab in refractory eosinophilic asthma

In a recent Lung Alert reviewing our study of mepolizumab in severe eosinophilic asthma,1 Barratt states that the study population represented a minority of patients with asthma and that they had corticosteroid-resistant disease.2 These comments require clarification. While we accept that the population studied by us represents a minority of patients with marked bronchodilator response and clinical exacerbation numbers of patients treated with mepolizumab (n=28) and placebo (n=32) for 50 weeks by tertile of response to prednisolone 0.5 mg/kg up to maximum of 40 mg/day given for 14 days and by tertile of response to inhaled salbutamol 200 µg. The response to prednisolone represents the change in post-bronchodilator FEV1 after salbutamol measured at the same time of day before and 1–2 h after the last dose of prednisolone. FEV1 was measured before and 20 min after inhalert and salbutamol. The values in the table represent the improvement in FEV1 before prednisolone and before randomisation to mepolizumab or placebo.

### Table 1 Exacerbation numbers by tertile of response to prednisolone and salbutamol

<table>
<thead>
<tr>
<th>Exacerbation no/patient/50 weeks</th>
<th>Change in FEV1 after prednisolone (ml)</th>
<th>Change in FEV1 after salbutamol (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>2.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Placebo</td>
<td>2.0</td>
<td>2.9</td>
</tr>
</tbody>
</table>

Oxygen or ventilation during flight for patients with neuromuscular disease?

We read with great interest the paper by Mistry et al.3 which analysed hypoxic challenge flight assessments in patients with restrictive disorders. In their study they dispute the current British Thoracic Society recommendations, demonstrating that, in this subgroup, all patients planning air travel should have a pre-flight evaluation because, even in patients with normal baseline arterial oxygen tension (PaO2) can fall below 6.6 kPa during hypoxic challenge.

We wanted to establish whether patients with restrictive disorders (with no lung disease) should be ventilated rather than oxygenated when they are hypoxic during flights. In fact, as has been shown by Masa et al.,2 only nasal ventilation and not oxygen can normalise baseline nocturnal alveolar hyperventilation in patients with chest wall diseases.

Our group has previously evaluated oxygenation during real flights in healthy subjects,3 demonstrating a mean (SD) oxygen saturation of 12.8 (6.5)% in long-distance flights (>2 h) and 4.2 (2.6)% in short-distance flights (<2 h).

We have recently studied two patients with neuromuscular disease during a flight from Porto to Barcelona (duration approximately 1 h 50 min). The first patient was an ambulatory 36-year-old woman with mitochondrial myopathy with a vital capacity (VC) of 400 ml (14%) and the ability to perform air stacking to a maximal inflation capacity (MIC)4 of 1070 ml (52%). The second patient was a 50-year-old quadriplegic post-polio man with a VC of 560 ml (18%) and an MIC of 1110 ml (35%). Both patients were on continuous non-invasive ventilation (NIV) with a volume-cycled ventilator (mean tidal volume 1200 ml) through a 15 mm mouthpiece during the day and a nasal mask during sleep.

The average SaO2 for the first patient was 97.9%, time with SaO2 <90% was 1.8 min and the minimum SaO2 was 81% (figure I). For the second patient, the average SaO2 was 97%, time with SaO2 <90% was 1.6 min and the minimum SaO2 was 84% (ventilator disconnection during micturition). The first patient needed to use a manual resuscitator connected to her mouthpiece to maintain adequate ventilation while the battery of her ventilator battery was being changed. Neither patient experienced respiratory distress during the entire flight and both returned home uneventfully.

In conclusion, when patients with restrictive disorders are correctly ventilated (even with a manual resuscitator) they may fly safely, with oxygen saturation profiles identical to healthy subjects, and may not need supplemental oxygen.

I D Pavord,1 P Haldar,1 P Bradding,2 A J Wardlaw2

1Institute for Lung Health, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester LE3 9QP, UK; University of Leicester, Leicester, UK

REFERENCES


Correspondence to  Professor I D Pavord, Institute for Lung Health, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester LE3 9QP, UK; ian.pavord@uhl-tr.nhs.uk

Competing interests None.

PostScript

Table 1 Exacerbation numbers by tertile of response to prednisolone and salbutamol

<table>
<thead>
<tr>
<th>Change in FEV1 after prednisolone (ml)</th>
<th>Exacerbation no/patient/50 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>Mepolizumab</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>p Value</td>
</tr>
<tr>
<td>&gt;220</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
</tr>
</tbody>
</table>

Correspondence to  Professor I D Pavord, Institute for Lung Health, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester LE3 9QP, UK; ian.pavord@uhl-tr.nhs.uk

Competing interests None.

Provenance and peer review Not commissioned; not externally peer reviewed.

Accepted 9 July 2009

Thorax 2010;65:370. doi:10.1136/thx.2009.122697

REFERENCES

Lung alert

Longevity of alveolar macrophages allow sustained in vivo expression of the human α1-antitrypsin gene and amelioration of emphysema

This study describes the transduction of mouse pulmonary alveolar macrophages using an intratracheally instilled lentiviral vector. The transferred genes were expressed in vivo for the duration of the lifespan of the mouse. Labelling studies using bromodeoxyuridine (BrdU) revealed continued expression of the transgenes by alveolar macrophages present in the mouse lung at the time of infection, and not by those recruited after inoculation.

Using this method, a human α1-antitrypsin-expressing lentiviral vector (ET1αhAAT) was instilled into live immunocompetent mice. The result was stable and sustained secretion of human α1-antitrypsin protein primarily in the lung by alveolar macrophages augmenting murine α1-antitrypsin levels. A model of emphysema was induced in these mice and a control group by intratracheal installation of porcine pancreatic elastase. The control group consisted of immunocompetent mice previously infected with a lentiviral-mediated reporter transgene (EF1αGDP). The effects of elastase on lung compliance, area-weighted mean alveolar diameter (an index of airspace enlargement in emphysema) and its heterogeneity were significantly less in the ET1αhAAT-expressing mice compared with the EF1αGDP group (all $p<0.05$).

This study demonstrates longevity of pulmonary alveolar macrophages in mice, and challenges previously held views that they are short lived. Lentiviral transduction to achieve prolonged therapeutic secretion of human α1-antitrypsin in vivo may make them a potential target cell population for application of gene therapy.


Toni Jordan

Correspondence to Toni Jordan, Liverpool Heart & Chest Hospital, Liverpool, UK; Toni.Jordan@LHCH.nhs.UK

Thorax 2010;65:371. doi:10.1136/thx.2010.136275