Lung cancer in HIV infected patients

Since the beginning of the AIDS epidemic our group has contributed to improving the knowledge concerning the impact of HIV infection in the lung. Several of these contributions have been published in Thorax as editorials, original articles and a review. In continuing this effort, we have recently published in Thorax a review entitled “Lung cancer in HIV infected patients: facts, questions and challenges.” The main objective of this educational review was to alert pulmonologists to a possible increase in the incidence of lung cancer in the HIV-positive population and to underline the facts that lung cancer occurs particularly in young subjects, may be less directly related to smoking and is probably associated with a worse outcome. This review included 103 references which were almost all original articles, six of which were from our group. However, during the time between submitting it to Thorax and publication in the journal, another review on the same topic was also published by our group in Lung Cancer. Even though there are strong similarities between the content of these two articles, the form of them is totally different. Furthermore, the review published in Thorax contained 29 additional references which were discussed in the paper. Unfortunately, during the process of reviewing the proof we omitted to include the article in press in Lung Cancer. We wish to apologise to the Editor of Thorax and the readers of the journal for this omission.

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References

Safety and tolerability of three consecutive bronchoscopies after allergen challenge in volunteers with mild asthma

Ethical and safety considerations limit the design of studies with more than two consecutive fiberoptic bronchoscopies (FOB) in patients with asthma. We present data on the safety and tolerability of three consecutive bronchoscopies at baseline, and 24 h and 7 days after allergen provocation. The study included 15 volunteers with mild asthma (9 men and 6 women); median age 25 (range 19–46) years; percentage predicted forced expiratory volume in 1 s (FEV1) 97% (range 75.4–125.7%); and a mean provocative concentration of methacholine causing a 20% fall in FEV1 (PC20) of 2.1 (95% confidence interval (CI) 1.2 to 3.6) mg/ml at baseline FOB, 0.93 (95% CI 0.38 to 2.2) mg/ml at 24 h (p = 0.08) and 0.90 (95% CI 0.45 to 1.8) mg/ml at 7 days (p = 0.03) after the allergen challenge.

FOB was not associated with a significant fall in FEV1 at baseline (median FEV1 93.9% predicted (range 80–120.1%) before FOB and 92.8% predicted (73.6–119.0%) at discharge). However, there was a significant reduction in median (range) percentage predicted FEV1 after FOB performed both 24 h and 7 days after the inhaled allergen challenge: 94.9% (75.1–111.1%) before FOB and 85.5% (62.4–119%) at discharge, p = 0.04, 24 h post challenge; and 100.1% (70.56–119) before FOB, falling to 90.2% (66.2–119%) 7 days later, p = 0.009. We found a correlation between the percentage of instilled bronchoalveolar lavage volume recovered and change in FEV1 at discharge (r = 0.31, p = 0.04) when comparing combined data for all three bronchoscopies.

The median (range) pre-FOB oxygen saturation on room air was 99% (95–100%), with no significant change at discharge (97% (96–100%), p = 0.25). During FOB, the median (range) maximum oxygen saturation recorded was 99% (98–100%), whereas the minimum was 96% (92–100%). End procedure median (range) saturation was 98% (91–100%) on 2–4 l supplemental oxygen. Oxygen saturation on room air 10 min post procedure was maintained at a median (range) of 98% (95–99%).

The median (range) oxygen saturation pre-FOB on room air was 99% (96–100%) at 24 h after the allergen challenge and 97% (94–100%) at discharge (p = 0.02). The peak median (range) oxygen saturation recorded was 99% (98–100%) and the lowest level recorded was 96% (94–100%). The end median (range) saturation was 97% (93–100%) on 2–4 l of entrained oxygen, whereas the saturation on room air 10 min post procedure was 98% (94–100%).

The median (range) pre-FOB oxygen saturation was 98.5% (96–100%) at 7 days and 97.5% (96–100%) at discharge (p = 0.05). The highest recorded median (range) oxygen saturation was 99.5% (98.5–100%) and the lowest was 96% (92–98%). No clinical consequence as a result of desaturation was seen during the course of bronchoscopy.

We found no significant correlation between the change in oxygen saturation and the percentage volume of bronchoalveolar lavage recovered.

Table 1 summarises the effects of FOB on asthma control the day after bronchoscopy. FOB was associated with increased symptoms on all occasions. A significant fall in FEV1 was seen only after FOB that was preceded by an allergen challenge (p = 0.002) and was associated with the most significant increases in symptoms (p = 0.001) and corresponding drug usage (p = 0.004). None of these changes required treatment other than inhaled short-acting beta-2-agonists and all had resolved by the second day after FOB. Of the 15 volunteers, 12 returned for follow-up 2–6 weeks after the end of the study. The median (range) percentage predicted FEV1 was 99.88% (97–100%) at follow-up compared with 95.18% (75.41–114.8%) measured at the study entry screening visit. All 12 of these volunteers were still maintained on short-acting beta-2 agonists only and none reported clinical deterioration of asthma control in the weeks after the study.

Table 1 Summary of the effect of bronchoscopy on asthma control in terms of percentage predicted forced expiratory volume in 1 s, symptom scores and frequency of reliever drugs recorded the day before and the day after fiberoptic bronchoscopy

<table>
<thead>
<tr>
<th>FOB</th>
<th>Day before FOB*</th>
<th>Day after FOB*</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOB1</td>
<td>FEV1%</td>
<td>84.80 (69.06–120)</td>
<td>87.98 (63.71–113)</td>
</tr>
<tr>
<td>Symptom score</td>
<td>0 (0–4)</td>
<td>4.5 (5–10)</td>
<td>NS</td>
</tr>
<tr>
<td>Reliever drug frequency</td>
<td>0 (0–2)</td>
<td>1 (0–8)</td>
<td>0.02</td>
</tr>
<tr>
<td>FOB2</td>
<td>FEV1%</td>
<td>90.17 (67.10–120.4)</td>
<td>82.18 (56.25–111.9)</td>
</tr>
<tr>
<td>Symptom score</td>
<td>0 (0–4)</td>
<td>3 (0–5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Reliever drug frequency</td>
<td>0 (0–4)</td>
<td>2 (0–16)</td>
<td>0.004</td>
</tr>
<tr>
<td>FOB3</td>
<td>FEV1%</td>
<td>86.78 (69.06–125.0)</td>
<td>86.43 (68.71–120)</td>
</tr>
<tr>
<td>Symptom score</td>
<td>0 (0–10)</td>
<td>2 (0–7)</td>
<td>0.05</td>
</tr>
<tr>
<td>Reliever drug frequency</td>
<td>0 (0–10)</td>
<td>1 (0–7)</td>
<td>NS</td>
</tr>
</tbody>
</table>

FEV1, forced expiratory volume in 1 s; FOB, fiberoptic bronchoscopy; NS, not significant.

The data set presented in Table 1 is representative of the protocol followed and the procedure is performed by an experienced group of operators with dedicated aftercare, three consecutive bronchoscopies can be performed in volunteers with asthma, with no occurrence of adverse events. Any deterioration in asthma control seems to be related to increased airway hyper-responsiveness resulting from allergen provocation, combined with bronchoscopy.

*Values are median (range).

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College Trust Fund.

This study was sponsored by the Imperial

Dynabead separation, CELLection Pan Mouse

Specific primers and probes were designed for

Invitrogen). We used pre-developed PCR pri-

transcription was performed (Superscript III,

incubated the processed sputum cells for 3 h at

respectively, and a pre-incubation sample was

markers of cell activation (mRNA

Percoll gel density gradient centrifugation. Cell

sputum: (1) magnetic bead separation; and (2)

for isolating and enriching macrophages in

phage biology in the airways. To this end,

order to advance our understanding of macro-

sputum macrophages from human volunteers in

non-invasive method of recovering cells from the

induced sputum

Macrophage enrichment from

induced sputum

Since induced sputum has become a widely used

mechanical method of recovering cells from the

surfaces of the bronchial airways, isolating specific
cell populations will be necessary in order to learn

more about their specific role in innate immunity and

inflammation in the airways. Several studies have
demonstrated the ability to conduct ex vivo analyses

on sputum cells such as phagocytosis and surface

marker measurements, but these have not been

performed on isolated cell types. 1, 2

This study demonstrates the capability to isolate

sputum macrophages from human volunteers in

order to advance our understanding of macro-

phage biology in the airways. To this end, the
techniques that can enrich and isolate cells

without significant activation would prove exter-

mely useful. We compared two common methods

for isolating and enriching macrophages in

sputum: (1) magnetic bead separation; and (2)
Percoll gel density gradient centrifugation. Cell

purity and markers of cell activation (mRNA

tumour necrosis factor α (TNFα) and interleukin-

IL1β (IL1β)) were measured at various time

points in the isolation process.

Nine healthy subjects underwent induced

sputum. Sputum collection and sputum proces-

sputum macrophages were removed and incubated at 37

˚C for 1, 2 and 3 h, respectively, and a pre-incuba-
tion sample was also collected. The macrophages

were further pelleted and stored at −70°C. For

Dynabead separation, CELLection Pan Mouse

IgG Kit (Dynal, Norway) was used for immu-
nomagnetic separation of airway macrophages

coated with mouse monoclonal IgG2b HLA-DR

antibody (Diatec, Norway). Bead coating and

cell isolation was performed according to the

protocol from the manufacturer. The isolated
cells were incubated at 37°C for 1, 2 and 3 h,
respectively, and a pre-incubation sample was
also collected. The samples were further pelleted

and stored at −70°C. Total RNA was extracted

(Quagen) from all the cell samples and reverse

transcription was performed (Superscript III,

Invitrogen). We used pre-developed PCR

primers and probes for TNFα and the house-

keeping gene PGK (Applied Biosystems). Specif-

ic primers and probes were designed for

an inhaled coarse fraction particulate matter activate

airway phagocytes in vivo in healthy volunteers.


1 Alexis NE, Lay JC, Zeman KL, et al. In vivo particle

uptake by airway macrophages in healthy volunteers.

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