Effect of N-acetyl cysteine on thiol levels

We read with interest the article by Dr Bridge- man and colleagues on the effect of oral N-acetyl cysteine (NAC) on thiol levels in epithelial lining fluid (ELF) and lung tissue (July 1994;49:670–5). Their suggestion that NAC may not be the drug of choice to en- hance the glutathione antioxidant potential of the alveolus is reinforced by recent studies showing that COPD is not supported by their data, since levels of cysteine or glutathione in ELF, bronchoalveolar lavage (BAL) fluid, or lung tissue were not normalized in these patients. In addition, they did not perform functional measurements.

Several studies have investigated the anti- oxidative capacity of NAC, 600 mg daily. In healthy smokers significant decreases in levels of lactoferrin, ECP, and chemotactic activity of neutrophils in BAL fluid, and of myelo- peroxidase and elastase levels in serum, were found.1,2 Treatment with NAC, 200 mg twice or three times daily for more than one year, was associated with a decrease in the number of bacteria, especially in patients with COPD.3 The design of some of these studies precludes firm conclusions, but they at least suggest that conventional doses of NAC may influence the antioxidative capacity of the lung. This is of special relevance in those patients with a significantly disturbed pulmo- nary oxidative/antioxidative balance, such as patients with COPD and smokers. Indeed, Lundbäck et al recently showed that two years of treatment with NAC, 600 mg daily, re- duced the annual decline in FEV1, compared with a control group.4 This effect was most pronounced in smoking patients over 50 years of age with already considerably decreased FEV1.

Looking at the pharmacokinetic data, the authors showed in a group of patients consist- ing of smokers, ex-smokers and non- smokers that NAC, 600 mg daily for five days, increased levels of glutathione in BAL fluid by 180% 1–3 hours after the last dose (p<0.05), and by 24% 16–20 hours after the last dose (NS).5 This "transient" increase in antioxidants in the lung apparently does not preclude a decrease in oxidative stress, or an improvement in antioxidative capacity of the lung, or both.

AUTHORS’ REPLY We thank Drs Dekhuijzen and van der Haer for their interest in our paper. We do not, however, agree with their conclusions. Although the patients in whom the BAL fluid measurements of antioxidants were performed were not specifically chosen as having COPD, these patients were all smokers or ex-smokers, as stated in the text, and table 1 clearly in- dicates that some had airflow limitation as shown by the predicted values for FEV1. Thus, some of these patients had COPD. The results of measurements of thiol concentra- tions in BAL fluid and lung tissue indicate that even with high doses of N-acetyl cysteine, the plasma concentrations of thiols in patients with COPD were lower than in normal subjects. The lack of any significant changes in thiol concentrations in BAL fluid and lung tissue in this group of patients with minimal airflow limitation suggests that levels in lung and BAL fluid would be even lower in patients with severe COPD.

The purpose of our study was not to assess any "functional" measurements but simply, as stated in the title, to determine whether there was a significant increase in thiol concentra- tions in plasma, BAL fluid, and lung tissue following treatment with N-acetyl cysteine. We are aware of studies which sug- gest a decrease in exacerbation of symptoms in patients with COPD treated with N-acetyl cysteine. We are also aware, and state in the paper, that the beneficial effect on ex- acerbations of COPD has been shown in some, but not all, studies. The purpose of our study was to determine whether the possible beneficial effects of N-acetyl cysteine could be explained by a significant change in thiol concentrations – and hence the antioxidant potential – in BAL fluid and in the lungs.

Drs Dekhuijzen and van der Haer are clearly aware of our previous data. However, we were unable to sustain significant increase in glutathione levels in the lung or BAL fluid with high doses of N-acetyl cysteine. These studies therefore lead us to conclude that N-acetyl cysteine, even in high doses, failed to produce any sustained or significant increase in thiol concentrations in the lung. We must therefore seek an alter- native explanation for the beneficial effects of N-acetyl cysteine shown in some studies with patients with COPD.

CF STANFORD
Department of Medicine, KRINKH, PO Box 9516, 3034 CS, The Netherlands

Asthma publications

The incidence of asthma is high in most communities and possibly increasing,1 and is associated with considerable morbidity.2 However, systematic reviews and Cochrane Collaboration meta-analyses of asthma interventions have been limited, with the majority of evidence gathered from studies undertaken over the past two decades.3 Despite this, there is still considerable uncertainty about the best way to manage asthma in individuals of all ages and in the general community.4 This has been particularly true for the management of asthma in children, who are at high risk of developing severe and life-threatening asthma.5,6

2 Castle, Fuller R, Hall J, Palmer J. Serovet nationwide surveillance study: comparison of

Number (% of papers on each aspect of asthma research published in Thorax and the American Review of Respiratory Diseases (ARRD) in 1993

<table>
<thead>
<tr>
<th>Subject of paper</th>
<th>Thorax</th>
<th>ARRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy</td>
<td>8 (9)</td>
<td>35 (20)</td>
</tr>
<tr>
<td>General</td>
<td>27 (31)</td>
<td>77 (45)</td>
</tr>
<tr>
<td>Therapy</td>
<td>46 (53)</td>
<td>47 (27)</td>
</tr>
<tr>
<td>Housing</td>
<td>2 (2)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Environment</td>
<td>3 (3)</td>
<td>11 (6)</td>
</tr>
<tr>
<td>Total</td>
<td>86 (100)</td>
<td>173 (100)</td>
</tr>
</tbody>
</table>
Effect of N-acetyl cysteine on thiol levels.

P N Dekhuijzen and C L Van Herwaarden

Thorax 1995 50: 215
doi: 10.1136/thx.50.2.215

Updated information and services can be found at:
http://thorax.bmj.com/content/50/2/215.1.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/