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Comparison of nebulised aerosol deposition in the lungs of healthy adults following oral and nasal inhalation

Mark L Everard, John G Hardy, Anthony D Milner

Abstract

A standard jet nebuliser was used to generate a radiolabelled aerosol and the pattern of deposition within the airways of eight healthy adults was studied with a gamma camera. Penetration of aerosol to the lung was greatly reduced when breathing through the nose compared with mouth breathing.

(Thorax 1993;48:1045–1046)

Although the nose acts as a filtration system it has been argued that patient preference should determine whether a facemask or a mouthpiece is used when inhaling aerosols from jet nebulisers.1 2 This argument is based on clinical studies which failed to show any significant difference in clinical response when salbutamol was inhaled through these two routes.3 However, bronchodilators are generally used in supramaximal doses4 and hence the observed clinical response need not directly reflect the total dose reaching the lungs. The dose of aerosol deposited in the lungs is determined by the total dose of drug inhaled and the pattern of deposition of that dose within the airways. The factors influencing the total dose of drug inhaled when using a jet nebuliser are complex and have previously been discussed.4 The purpose of this study was to determine what effect inhaling a wet, heterodispersed aerosol by the nasal rather than the oral route might have on the pattern of deposition within the airways. A standard technique5 6 was used in which the deposition of a radiolabelled aerosol was assessed with a gamma camera.

Methods

Eight men aged 21–32 years were studied. All were in good health, were non-smokers, and gave no history of lower respiratory tract dis-
ease or current rhinitis. Ethical committee approval was obtained for this study.

The subjects attended on two separate occasions separated by at least 48 hours. During each visit they inhaled a radiolabelled aerosol for 75 seconds. This was generated by a Cirrus nebuliser (Intersurgical) which had been filled with 2 ml normal saline radio-labelled with approximately 40 MBq ⁹⁹ᵐTc-labelled diethylenetriamine pentaacetate (DTPA). A driving gas flow of 8 l/min was used. Relaxed tidal breathing was used to mimic the clinical setting and subjects inhaled from a facemask in a random order either through their nose, or through their mouth while using a nose clip. The subjects used their own allocated nebuliser and, apart from the route of inhalation, the conditions were the same for both visits. The nebuliser was housed in a lead case and aerosol generated during the expiratory phase or exhaled was collected on a filter to avoid environmental contamination. Immediately after administration of the ⁹⁹ᵐTc-labelled aerosol a gamma camera was used to record anterior and posterior images of the chest and stomach together with a lateral image of the head and neck. These images were displayed on a television screen and areas of interest were defined. Count rates were determined for the lungs, stomach, lower oesophagus, nose, and oropharynx. Each count rate was corrected for background counts and the geometric means of the corresponding anterior and posterior count rates were calculated. The outlines of the lungs were delineated during one visit by obtaining a posterior image of the lungs while the subject inhaled 81m-labelled krypton gas.

The dose deposited in the lungs was then expressed as a percentage of the total dose deposited in the body. Deposition within the lungs was subdivided into three regions; central, mid, and peripheral. From the krypton images the dimensions of each lung were considered to be those of a matrix 8 × 5 units wide. A block of six cells defined the central region of the lung, and this was surrounded by a mid lung region one cell wide. The remaining cells defined the peripheral region.

A Malvern 2600 laser particle sizer with the Fraunhofer diffraction model was used to obtain the mass median diameter of the aerosol generated by the nebuliser under these conditions. This diameter is such that 50% of the droplet mass within the aerosol is contained in smaller droplets and 50% in larger droplets.

### Results

The quantity of aerosol deposited within the lungs as a percentage of the total dose deposited in the body is shown in the table. The mean improvement in lung deposition when breathing through the mouth was 37% (p < 0.01, Wilcoxon signed rank test). The mean deposition within the central, mid, and peripheral regions when expressed as a percentage of the total dose deposited in the lungs was 27%, 32%, and 41% after nasal breathing, and 28%, 32%, and 40% after inhalation through the mouth.

<table>
<thead>
<tr>
<th>Mass Median Diameter of 4.4 μm</th>
<th>82</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser particle sizer</td>
<td>82</td>
</tr>
</tbody>
</table>

### Aerosol deposition within the lungs as a percentage of total deposition within the body

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Nasal breathing</th>
<th>Mouth breathing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>79</td>
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<td>76</td>
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<td>85</td>
</tr>
<tr>
<td>7</td>
<td>34</td>
<td>70</td>
</tr>
<tr>
<td>8</td>
<td>37</td>
<td>70</td>
</tr>
</tbody>
</table>

(range 3-8-51 μm) was obtained for the nebulisers used in this study when a driving gas flow of 8 l/min was used.

### Discussion

This study with a radiolabelled wet aerosol from a jet nebuliser shows that there is considerable intersubject variation in the ability of the upper airway to filter out droplets when inhaled by either the oral or nasal route even in fit healthy volunteers. Despite using a high driving gas flow, the proportion of the dose deposited in the upper airway was substantially greater for all subjects when inhaling through the nose than through the mouth. This is not entirely surprising since workers in the field of industrial hygiene, using monodispersed aerosols, have shown that nasal deposition increases with increasing inspiratory flow rates and increasing particle size. It has been estimated that at an inspiratory flow rate of 30 l/min, nasal trapping increases from 10% for particles of 1 μm diameter to more than 90% for 10 μm particles. They have also shown that a mouthpiece can further reduce upper airways deposition by reducing deposition within the oral cavity. For many drugs delivered via jet nebulisers such as antibiotics, steroids or, indeed, those used in bronchial challenges such as histamine, the clinical response is likely to correlate closely with the dose reaching the lungs. In these situations oral breathing, preferably via a mouthpiece, is to be recommended.

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