Reduction in nitrogen dioxide concentration by soda lime preparations during simulated nitric oxide inhalation

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Summary
Nitrogen dioxide is formed during delivery of inhaled nitric oxide for the treatment of patients with pulmonary hypertension. Soda lime has been shown to absorb nitrogen dioxide. We tested three different commercially available soda lime preparations (Sodasorb, Drägersorb 800 and Sofnolime) for their efficacy in absorbing nitrogen dioxide and nitric oxide during simulated nitric oxide inhalation. All soda lime preparations absorbed nitrogen dioxide (15%, 24% and 34%, respectively). To test if this difference could be attributed to the potassium hydroxide (KOH) content of the different preparations, two other preparations with a higher (3.0% and 7.3% w/w, respectively) KOH content were tested and we found an increase in nitrogen dioxide removal up to 47% and 46%, respectively. We conclude that soda lime absorbed nitrogen dioxide during nitric oxide inhalation. This effect seemed to be moderate under simulated clinical conditions, but increased using soda lime with a higher KOH content. Nevertheless, we recommend continuous monitoring of inspired nitrogen dioxide concentration during clinical inhalation of nitric oxide. (Br. J. Anaesth. 1997; 79: 641–644).

Key words

Inhaled nitric oxide gas is a selective pulmonary vasodilator which has been used to treat persistent primary pulmonary hypertension of the newborn,1 primary pulmonary hypertension,2 ARDS,3 and pulmonary hypertension in congenital heart diseases4 and after cardiac surgery.5 Potential side effects of this therapy include methaemoglobinaemia and formation of toxic nitrogen dioxide.

Nitric oxide is oxidized rapidly to nitrogen dioxide in the presence of oxygen. The amount of nitrogen dioxide formed depends on the concentration of nitric oxide and oxygen in the gas mixture, and the time available for the reaction. We have demonstrated previously that the amount of nitrogen dioxide formed during nitric oxide inhalation correlated with the inspired nitric oxide concentration, the fraction of inspired oxygen and the minute volume delivered by the ventilator.6 Nitrogen dioxide concentrations up to 2.0 parts per million (ppm) were encountered.

It has been recommended as a safety standard that nitrogen dioxide concentrations should be monitored during inhalation of nitric oxide,7 8 but a maximum tolerable concentration of nitrogen dioxide during clinical administration of inhaled nitric oxide has not yet been defined. The Centers for Disease Control recommend an upper limit of 5 ppm of nitrogen dioxide for occupational health.9 However, inhalation of lower nitrogen dioxide concentrations has been demonstrated to increase airway resistance,10 reduce mucociliary activity11 and impair host defence12 in humans. Animal studies showed morphological changes such as loss of cilia, hypertrophy and hyperplasia of the bronchial epithelium, thickening and fibrosis of alveolar septa, and emphysema after long-term exposure.13–15 Studies on the pulmonary effects of nitrogen dioxide in critically ill patients are not available.

In 1967 contamination of nitrous oxide cylinders with high concentrations of nitric oxide and nitrogen dioxide led to deleterious complications during general anaesthesia16 and prompted a study by Kain which demonstrated for the first time the ability of soda lime to absorb nitrogen dioxide.17 Recently, a few conflicting reports have been published showing complete,18 marked19 or no nitrogen dioxide absorption20 by soda lime. Some of these studies were performed by passing a constant gas flow through soda lime cylinders,18 20 while other authors tested soda lime with delivery systems used clinically.19

This study was designed to investigate the efficacy of three soda lime preparations in absorbing nitrogen dioxide and nitric oxide in a clinical setting. As the major difference in the chemical composition of these soda lime preparations is the potassium hydroxide (KOH) content, we also tested the hypothesis that nitrogen dioxide absorption could be increased by increasing the KOH content of soda lime.
Methods

A mechanical lung simulator (Drägerwerk AG, Lübeck, Germany) was ventilated in a volume-controlled mode using an Evita 2 ventilator (Drägerwerk AG, Lübeck, Germany) at a constant rate of 12 bpm (fig. 1). A commercially available ventilator tubing set (polyethylene tubes with a diameter of 2.1 cm; B+P Beatmungsschläuche GmbH, Neunkirchen/Seescheid, Germany) was used in the inspiratory (length 240 cm) and expiratory (length 200 cm) limbs with a water trap in each limb connected via a Y-piece to the lung simulator.

Nitric oxide was delivered from a gas cylinder containing nitric oxide 1000 ppm in pure nitrogen (AGA, Lidingö, Sweden) into the inspiratory limb using a nitric oxide delivery device (NODOMO) (Drägerwerk AG, Lübeck, Germany). In order to maintain the nitric oxide concentration stable, the NODOMO adjusts nitric oxide flow proportionally to the flow of the ventilator.

We measured nitrogen dioxide and nitric oxide concentrations by chemiluminescence (CLD 700 AL, Zellweger-Eco-Systeme GmbH, Rösrath, Germany) in the inspiratory limb, 80 cm before the Y-connector. To prevent pressure-induced instability of the measurements caused by positive pressure ventilation, a pump was used to sample gas from the inspiratory limb. The gas sampling line of the CLD 700 AL was connected to a Y-piece at the outlet of the pump. Setting the suction rate of the pump higher than that of the CLD 700 AL ensures pressure-constant gas sampling by the CLD 700 AL. Calibration was performed after every 8 h of measurement with a gas mixture containing nitric oxide 30 ppm and nitrogen dioxide 7 ppm in pure nitrogen (AGA, Lidingö, Sweden).

An acrylic soda lime cylinder (Drägerwerk AG, Lübeck, Germany) with a diameter of 9 cm and a height of 12 cm (764 ml) was introduced into the inspiratory limb 80 cm beyond the ventilator. To achieve different nitrogen dioxide concentrations, we changed settings for minute ventilation (\(\dot{V}e\)) (5, 10 litre min\(^{-1}\)), fraction of inspired oxygen (\(F_{o_2}\)) (0.25, 0.75, 0.99) and nitric oxide concentration (20, 40, 80 ppm). Measurements were obtained with (+SL) and without (−SL) soda lime leading to a single data pair for each setting.

SODA LIME PREPARATIONS

We evaluated three different commercially available soda lime preparations for their ability to reduce nitrogen dioxide and nitric oxide concentrations: Sodasorb (WR Grace Co., Lexington, USA), Drägersorb 800 (Drägerwerk AG, Lübeck, Germany) and Sofnolime (Molecular Products Ltd, Thaxted, Essex, UK). Additionally, two soda lime preparations with a higher concentration of KOH were tested: Special-1 and Special-2 (Molecular Products Ltd, Thaxted, Essex, UK).

The soda lime preparations did not differ in colour indicator (ethyl violet) or granule size (4.0–8.0 mm in diameter). The chemical composition of the soda limes is given in table 1.

### Table 1  Chemical composition of the soda lime preparations tested

<table>
<thead>
<tr>
<th>Soda lime</th>
<th>Hydroxide content (% w/w)</th>
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<tbody>
<tr>
<td></td>
<td>Calcium</td>
</tr>
<tr>
<td>Sodasorb</td>
<td>48.0</td>
</tr>
<tr>
<td>Drägersorb 800</td>
<td>45.0</td>
</tr>
<tr>
<td>Sofnolime</td>
<td>46.0</td>
</tr>
<tr>
<td>Special-1</td>
<td>44.0</td>
</tr>
<tr>
<td>Special-2</td>
<td>44.0</td>
</tr>
</tbody>
</table>

DATA ANALYSIS

Paired values were plotted in a scatterplot (values without soda lime (−SL) on the X-axis and corresponding values with soda lime (+SL) on the Y-axis). Linear regression was performed leading to the standard equation \(y = mx + b\) of the fitted straight line. The difference between unity and the slope (\(m\)) of this line represents the efficiency of nitrogen dioxide or nitric oxide removal by the particular soda lime. \(r^2\) values were calculated to test the strength of the linear correlation.
Results

During administration of inhaled nitric oxide up to 80 ppm, nitrogen dioxide concentrations of up to 2.0 ppm were measured. The amount of nitrogen dioxide formed depended on the ventilatory setting: the higher the concentrations of inhaled nitric oxide and $F_{\text{NO}_2}$ and the lower the minute ventilation, the higher were the measured nitrogen dioxide concentrations.

Values of nitrogen dioxide and nitric oxide concentrations with and without soda lime showed a strong linear correlation, as indicated by $r^2$ values always exceeding 0.9.

All soda lime preparations reduced nitrogen dioxide concentration. Nitrogen dioxide absorption ranged from 15% (Sofnolime) to 34% (Drägersorb 800) for the commercially available soda limes and was higher for Special-1 (47%) and Special-2 (46%) (fig. 2).

While Sodasorb did not absorb nitric oxide, we found a slight reduction in nitric oxide concentration with Drägersorb 800 (2%), Sofnolime (3%), Special-1 (8%) and Special-2 (7%), respectively (fig. 2).

Discussion

We have demonstrated that three soda lime preparations (Sodasorb, Drägersorb 800 and Sofnolime) absorbed nitrogen dioxide formed during simulated ventilation with nitric oxide. Nitrogen dioxide absorption varied from 15% to 34% while nitric oxide absorption was 0–2%.

In contrast with our study, Stenqvist, Kjelltoft and Lundin\textsuperscript{19} demonstrated a reduction in nitrogen dioxide concentrations in the inspiratory limb of their nitric oxide ventilatory system by almost 80%, but a different soda lime preparation (Q-sorb) and a larger soda lime cylinder (900 ml) were used. Ishibe and colleagues\textsuperscript{18} showed complete absorption of nitrogen dioxide and 25% (Soda sorb) and 29% (Wako lime-A) absorption of nitric oxide using two types of soda lime. The high absorptions in the study of Ishibe and colleagues\textsuperscript{18} may be explained by the long contact time between the gas mixtures and soda lime, resulting from a low and constant flow (1 litre min$^{-1}$) through the soda lime column (145 ml). Using a constant gas flow of 10 litre min$^{-1}$, which is more likely to represent clinical conditions, Pickett and colleagues\textsuperscript{20} tested three different soda lime preparations. They found a marked reduction in nitrogen dioxide concentrations (80.6% and 83.9%) and a lesser reduction in nitric oxide concentrations (13.3% and 12.7%) by two types of soda lime. With a third type, both nitrogen dioxide and nitric oxide were absorbed completely as a result of an oxidizing indicator (potassium permanganate). Indicators used in commercially available soda lime preparations have no oxidizing properties. Therefore, the size of the soda lime cylinder, type (constant vs intermittent) and rate of gas flow through the cylinder, and chemical properties of the indicator may determine the amount of absorption of nitrogen dioxide and nitric oxide.

As the only difference between the three commercially available soda lime preparations was the concentration of potassium hydroxide (KOH), we hypothesized that the difference in nitrogen dioxide absorption may be related to the concentration of KOH. Therefore, we tested two soda lime preparations with an increased KOH content (Special-1 and Special-2). We found that nitrogen dioxide absorption increased to 47% and 46%, respectively. Nitric oxide removal was increased to a maximum of 8% (Special-2). Extending the reactions suggested by Kain\textsuperscript{17} and Ishibe and colleagues,\textsuperscript{18} the following chemical reactions during absorption of nitrogen dioxide and nitric oxide by soda lime may occur:

\[4\text{NO} + 4\text{NO}_2 + 4\text{NaOH} + 2\text{Ca(OH)}_2 + 4\text{KOH} \rightarrow 2\text{NaNO}_2 + 2\text{NaNO}_3 + \text{Ca(NO)}_3 + \text{Ca(NO)}_3 + 2\text{KNNO}_3 + 2\text{KNNO}_3 + 4\text{H}_2\text{O}\]

It is known that the radii of the hydroxides of group I elements decrease when the radius of the ion itself increases. This may account for the higher reactivity of the larger ions. As the sodium ion is smaller than the potassium ion, KOH may be more potent in binding nitric oxide or nitrogen dioxide. However, the exact mechanism by which KOH
improves nitrogen dioxide absorption remains to be elucidated.

Increasing the KOH content of soda lime may be limited by the known effect of “caking”, especially when humidifiers are used. How the use of humidifiers may affect nitrogen dioxide and nitric oxide absorption by soda lime is not known. In one pilot experiment (unpublished data) we measured an increase in formation of nitrogen dioxide by approximately 30% when a humidifier was introduced into the inspiratory limb. Absorption of nitrogen dioxide and nitric oxide using Drägersorb 800 did not seem to be affected when measured over 10 min.

Other materials such as molecular sieve 5A and charcoal have been evaluated for their ability to reduce nitrogen dioxide and nitric oxide concentrations, but they lack specificity for nitrogen dioxide. While occupational exposure to nitric oxide and nitrogen dioxide in intensive care units has been shown to be low, these and other non-selective scavengers of nitric oxide and higher nitrogen oxides were recommended to avoid environmental pollution during nitric oxide inhalation.

As the dust from soda lime-containing hydroxide salts is irritating to skin and mucous membranes, the use of soda lime absorbers, as in anaesthesia systems, is essential.

We conclude that commercially available soda lime absorbed nitrogen dioxide formed during inhalation of nitric oxide. Although an increase in KOH content increased nitrogen dioxide removal, complete elimination of nitrogen dioxide from the inspired gas mixture could not be achieved. Therefore, soda lime may be helpful in preventing delivery of high nitrogen dioxide concentrations under specific clinical conditions, but continuous monitoring of inspired nitrogen dioxide concentration remains mandatory when nitric oxide inhalation is required.

Acknowledgement

We thank Molecular Products Ltd for supplying the soda lime preparations Sofnolime, Special-1 and Special-2.

References