Is the short term limit value for sulphur dioxide exposure safe? Effects of controlled chamber exposure investigated with bronchoalveolar lavage

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ABSTRACT Bronchoalveolar lavage (BAL) which has not previously been used in investigating the effect of sulphur dioxide (SO2) on the human lung was performed on 12 subjects before and after controlled chamber exposure with SO2 for 20 minutes. BAL fluid 24 hours after exposure with 10 mg SO2/m3 (4 ppm, 10 subjects) showed increased alveolar macrophage activity as judged by an increase in lysozyme positive macrophages. Twenty four hours after 20 mg/m3 (4 subjects) a further increase was seen, which was accompanied by an increase in total numbers of macrophages and lymphocytes. Seventy two hours after exposure (4 subjects) cell numbers had virtually returned to pre-exposure levels. These previously uninvestigated reactions indicate potentially noxious effects of SO2 in the lungs at exposure levels that are regarded as relatively safe.

Sulphur dioxide (SO2) is a gas that is rapidly oxidised to sulphuric acid in contact with moist epithelial surfaces in the eyes, nasopharynx, and lower airways, where it may cause damage. It is a major air pollutant in urban areas, particularly in the working environment of pulp industries and factories using various combustion and smelting processes. High peak exposures, many times exceeding the Swedish short term exposure limit of 13 mg SO2/m3 air (5 ppm), have been frequently found1 (and N Stjernberg et al, unpublished data). Similar findings have been reported in other countries.13 Pulmonary effects of SO2 in man have mainly been studied indirectly by lung function tests,15 tests of hyperreactivity,6 and in epidemiological surveys17 (and N Stjernberg et al). Direct investigation has been restricted to workers who have died of massive exposure to SO2, in whom gross histopathological changes in the lung tissue with haemorrhagic alveolar oedema have been reported.14 Bronchoalveolar lavage (BAL), which is a commonly used method for investigating conditions at the alveolar level has not to our knowledge previously been used for studying SO2 effects in man.

Our aim, using the BAL technique, was to determine if short term exposure to SO2 in concentrations around the Swedish short term exposure limit, concentrations which are commonly found in industrial environment, causes potentially harmful effects on the alveolar cell population.

Subjects and methods

Subjects

Twelve healthy, non-smoking subjects, aged 22-30 (mean 24) participated in this investigation. None had a history of airway infection for at least six weeks before BAL or a history of bronchial hyperreactiveness. Pre-exposure lung function and gas distribution were normal in all subjects.

SULPHUR DIOXIDE EXPOSURE

The exposure chamber measured 3.20 × 2.00 × 2.20 m with an air volume of 14.1 m3. It was built of anodised aluminium with windows in one wall. Ambient air was drawn continuously through the chamber at 400 m3/h, resulting in one air exchange about every two minutes. Pre-exposure measurements have shown low levels of particulate matter in the chamber. During exposure, the chamber air temperature was kept at 20°C and the relative humidity around 50%. The concentration of SO2 in the exposure chamber was controlled by adding a gas stream from a 1% SO2 gas tube to the chamber air inlet. The chamber air was continuously analysed with an electrochemical method in which SO2 is oxidised to...
SO₂ effects investigated with bronchoalveolar lavage

Cell numbers in bronchoalveolar lavage fluid after controlled exposure to sulphur dioxide. Data are given as median with range

<table>
<thead>
<tr>
<th>Time after exposure</th>
<th>Total cell count × 10⁴/l</th>
<th>Lymphocytes × 10⁴/l</th>
<th>%</th>
<th>Macrophages/monocytes × 10⁴/l</th>
<th>%</th>
<th>Lysozyme positive macrophages/monocytes × 10⁴/l</th>
<th>% of macrophages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before exposure</td>
<td>6-9 (2-17-4)</td>
<td>0-3 (0-1-2-6)</td>
<td>6</td>
<td>6-3 (11-8-14-3)</td>
<td>92</td>
<td>0-4 (0-1-3-4)</td>
<td>5</td>
</tr>
<tr>
<td>24 h after 10 mg SO₂/m³ (n = 10)</td>
<td>6-0 (1-4-14-0)</td>
<td>0-5 (0-1-1-3)</td>
<td>7</td>
<td>4-9 (1-3-12-3)</td>
<td>91</td>
<td>0-8 (0-1-1-5)</td>
<td>14</td>
</tr>
<tr>
<td>24 h after 20 mg SO₂/m³ (n = 4)</td>
<td>16-0 (8-6-21-0)</td>
<td>3-1 (1-2-5-9)</td>
<td>20</td>
<td>12-4 (6-8-14-3)</td>
<td>76</td>
<td>2-6 (1-5-4-6)</td>
<td>18</td>
</tr>
<tr>
<td>72 h after 20 mg SO₂/m³ (n = 4)</td>
<td>8-2 (7-0-12-2)</td>
<td>1-0 (0-5-1-5)</td>
<td>12</td>
<td>7-1 (5-8-11-2)</td>
<td>88</td>
<td>0-5 (0-4-2-1)</td>
<td>7</td>
</tr>
</tbody>
</table>
cells, and the ratio of helper-inducer/suppressor-
cytotoxic T cells, were within normal limits and were
not significantly changed after exposure. The counts
for lymphocytes and macrophages/monocytes are
given in the table.

Twenty four hours after exposure to 10 mg SO2/m3
there was an increase in lysozyme positive
alveolar macrophages (Lys+MF) in total number and
in per cent of the total amount of alveolar macro-
phages (Tot-MF) compared with values before
exposure (p < 0.01 respectively).

Twenty four hours after exposure to 20 mg SO2/m3
Lys+MF were further increased, both in per cent of
Tot-MF and in total number. Tot-MF and the total
cell number were also increased. A mild lymphocytosis
was also seen, with a median value of 20% (range 12–
28%) as compared with 6% (range 2–18%) before
exposure. The total number of lymphocytes in BAL
was two to four times higher than before exposure. An
increase in the numbers of macrophages and lympho-
cytes was found in all four subjects.

Seventy two hours after exposure to 20 mg SO2/m3
lymphocytes, Lys+MF, Tot-MF, and total cell
numbers had virtually returned to pre-exposure levels.

LUNG FUNCTION
Vitalograph recordings before, immediately after, and
15 minutes after exposure to SO2 showed no significant
decrease in lung function. Similar results were
obtained 24 and 72 hours after exposures immediately
before BAL.

SYMPTOMS
The subjects reported mild symptoms from the eyes
and nose during exposure. All denied symptoms from
the eyes or airways after exposure.

Discussion
Sulphur dioxide is a common environmental pollutant1
and large numbers of factory workers worldwide
are frequently exposed to levels well exceeding
the short term exposure limits, which vary between 10
and 20 mg SO2/m3 in the industrialised countries.3
Until now, the effects of short term exposure of SO2
on the human lung have not been investigated by a direct
technique such as BAL.

The SO2 exposure levels in the present study are
based on previous measurements in pulp industry
works and are equal to the upper and lower range of
short term exposure limits in industrialised coun-
tries12 (and N Stjernberg et al). The controlled
chamber exposures were designed to simulate the
work conditions in the type of industries in which
exposure to SO2 is frequent and particulate levels low.
The workers in these industries are mainly occupied
with supervising chemical processes but are frequently
exposed to peak levels of SO2 during short periods
when they check and adjust the machinery. This
workload is mainly light to moderately heavy which
why we chose 75 W on the ergometer bicycle. The
workload also means that the workers are not forced
to breathe much through the mouth.1 This is benefi-
cial, since the exposure of lower airways to SO2 is
distinctly higher during oral breathing than during
nasal breathing and rapidly increases with increased
airflow. Approximately 98% of SO2 had been found to
be absorbed in the nasopharynx during nasal breathing.13,14 Even though the doses of SO2 that reach the
alveoli appear to be small the cell reactions in BAL
fluid indicate noxious effects at this level of the
airways, by contrast with the mild symptoms from the
upper airways and absence of airflow obstruction.

Lysozyme positivity is a property of monocytes
and newly recruited to the alveoli and is usually lost when
they have matured to macrophages.15 Lysozyme in
macrophages is also believed to be a marker of cell
activation and may be increased by a variety of stimulii.16,17 After the low exposure to SO2, 10 mg/m3
Tot-MF was unchanged while the relative numbers of
Lys+MF were increased. This indicates that the Lys+
MF seen in BAL had not migrated from the blood
stream after the exposure but were residing alveolar
macrophages who had reacted to the SO2 stimulus
with lysozyme production. Twenty four hours after 20
mg SO2/m3, however, a migration to the alveoli
appears to have taken place. That that alveolar
macrophage activation was the only observed cellular
reaction after the low exposure level may indicate that
this is a prime target cell for SO2. Macrophages also
have the ability to induce lymphocyte chemotaxis and
proliferation by release of mediators such as Inter-
leukien-1 and could thus induce the lymphocytosis
observed after exposure to 20 mg SO2/m3. Interest-
ingly, this lymphocytosis was not accompanied by
any change in the ratio between Leu 2/Leu 3 positive
lymphocytes. This may indicate that the lympho-
cytosis was mainly due to lymphocyte chemotaxis and
not primarily to a proliferative response.

BAL after controlled chamber exposure with gas-
eous pollutants seems to be a useful method for
evaluation of effects at the alveolar level of the lungs.
BAL, 24 hours after short term exposure with 10 mg
(ppm) and 20 mg SO2/m3 (8 ppm), showed increased
alveolar macrophage activity and at the higher dose
also a mild lymphocytosis that had virtually returned
to normal 72 hours after exposure. These previously
uninvestigated reactions indicate potentially noxious
effects of SO2 in the lungs at exposure levels that are
presently regarded as relatively safe. Further studies
are in progress to evaluate the effects of SO2 in the
lungs of man.
SO₂ effects investigated with bronchoalveolar lavage

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References


14 Frank NR, Yoder RE, Brain JD, Yokoyama E. SO₂ (35S labeled) absorption by the nose and mouth under conditions of varying concentration and flow. Arch Environ Health 1969;18:315–22.

