Effect of Ultrasonic Nebulization on Blood Gas Tensions in Chronic Obstructive Lung Disease

James T. Taguchi, M.D.*

Ultrasonic nebulization therapy (U/air) resulted in a decline in PaO₂ of -5 to -22 mm Hg in ten of 15 chronic obstructive lung disease (COLD) patients. A similar decline in PaO₂ occurred in four of ten COLD patients when ultrasonic nebulization was given with intermittent positive pressure breathing (IPPB [IPPB/U/air]). Complaints of discomfort from treatment were elicited in ten of 15 COLD patients treated with U/air and all ten COLD patients treated with IPPB/U/air. No consistent correlation of symptoms with the changes in PaO₂ was noted. The increase in airway resistance with ultrasonic nebulization which occurs only in patients with COLD probably best explains the complaints, since our control patients had a greater incidence and degree of PaO₂ decline and yet remained free of discomfort. Respiratory alkalosis was noted in one of 15 and three of ten COLD patients treated with U/air and IPPB/U/air, respectively. Hypoventilation with a decrease in PaO₂ and pH and a rise in PaCO₂ occurred in two patients receiving U/air. The mechanisms for the reduction in PaO₂ are complex, including hypoventilation, increased workload of breathing, and most commonly, ventilation perfusion abnormalities. Acute blood gas changes are common with ultrasonic therapy and have important clinical implications which must be evaluated along with other known hazards of inhalational therapy.

Inhalational therapy has become an extremely popular therapeutic measure with an increasing number of patients being treated for bronchopulmonary diseases, as well as for the prevention of bronchopulmonary disorders following surgery. A further impetus to inhalational therapy has been the addition of ultrasonic nebulization, which is reported to be capable of delivering large quantities of moisture to the lower tracheobronchial tree, thus enhancing bronchial toiletry.1–5

We have observed that many of our patients with chronic obstructive lung disease (COLD) complain bitterly or even refuse inhalational therapy because of accompanying discomfort, especially when ultrasonic therapy is delivered via intermittent positive pressure breathing (IPPB). Studies have shown that artificial fog and ultrasonic nebulization will cause an increase in airway resistance,6–8 but we were concerned about the blood gas changes, especially in hypoxic patients and whether they were related to symptoms.

### Materials and Methods

Blood gas data were studied in 20 hospitalized patients who were receiving ultrasonic treatment in the Inhalational Therapy Department. Five patients did not have COLD (group 1). Two of the patients in this group had had acute bronchitis and were asymptomatic at the time of the study. Two were patients with bronchogenic carcinoma, and the fifth patient had rheumatic heart disease with no evidence of lung disease. This heterogenous group was considered as the "control" group. Their baseline ventilatory and gas values are compared with those of the 15 patients with COLD in Table 1. Fifteen patients had COLD of moderate to very severe degree. Ten of these 15 had normal resting Paco₂ (group 2) and five (group 3) had hypercapnia with Paco₂ values ranging from 49 to 60 mm Hg.

Their pulmonary disease status was stable at the time of the study. Ventilatory measurements of FEV₁, MVV, RV, TLC, and nitrogen washout were obtained before beginning the blood gas studies in nearly all the patients. Several patients were unable to cooperate sufficiently for satisfactory ventilatory studies.

A Cournand needle was inserted in the brachial artery for serial sampling. All samples were drawn anaerobically in heparinized syringes and immediately placed in ice. Duplicate determination were checked within ± 0.5 mm Paco₂, ± 1 mm Po₂ and ± .01 pH on a blood gas analyzer.† Patients

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†Model 113 Blood Gas Analyzer, Instrumentation Laboratory, Inc, Lexington, Mass.
were all in a seated position, and following the baseline blood gas measurements, ultrasonic therapy was administered via an Ohio face tent with a DeVilbiss ultrasonic nebulizer for a 20-minute period, utilizing a high setting of approximately four microliters per minute with isotonic saline as the nebulizing agent.

Specimens for blood gas studies were then drawn at 10- and 20-minute intervals during therapy and then 30 and 60 minutes after therapy had been discontinued. At the end of the treatment, the technician or the physician completed a questionnaire which was designed to assess subjective results of treatment and any side effects.

These blood gas studies were repeated in 15 of the 20 patients, with ultrasonic therapy being administered via a mouthpiece with intermittent positive pressure breathing (IPPB/U/air) at 15 cm of air pressure. Five patients were unable to tolerate the addition of IPPB and refused to proceed with the study. The initial form of therapy was alternated so that some patients were initially treated with ultrasonic (U/air) and the others with IPPB/U/air.

**RESULTS**

For the purpose of this study, a change of 5 mm or greater from the baseline PaO2 and PaCO2 was considered significant. With ultrasonic treatment alone (U/air) a drop in PaO2 ranging from −5 to −22 mm Hg occurred in all five patients in group 1 (Fig 1), six of ten in group 2 (Fig 2), and four of five in group 3 (Fig 3). With ultrasonic therapy delivered by IPPB/U/air, a drop in PaO2 ranging from −5 to −19 mm Hg developed in three of five in group 1, three of seven in group 2, and one of three in group 3. With both U/air and IPPB/U/air, the maximum decrease in PaO2 first appeared occasionally at 10 minutes of treatment, usually by 20 minutes, and often following treatment. It should be noted that five patients in groups 2 and 3 either refused or were unable to complete IPPB/U/air therapy because of discomfort produced by the addition of IPPB, and blood gas studies could not be obtained.

A rise in PaCO2 with a drop in pH accompanied the drop in PaO2 with U/air therapy in two of the 20 patients studied and both occurred in patients with COLD. One was a patient in group 3 with a baseline PaCO2 of 49 and pH of 7.40. This patient developed a decrease in pH to 7.32 and rise in PaCO2 to 50 (Fig 4). A decrease in PaCO2 preceded the drop in PaO2 in one patient each in group 1 and group 2 and was associated with a pH of 7.48 and 7.63, respectively. Figure 5 demonstrates the sequence of blood gas changes in the COLD patient in group 2 and shows a similar sequence with IPPB/U/air but without a decline in PaO2.

None of the 15 patients treated with IPPB/U/air

**Model 800-880 DeVilbiss Ultrasonic Nebulizer, The DeVilbiss Company, Somerset, Penn.**

**Table 1—Baseline Blood Gas and Ventilatory Function.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (percent predicted)</td>
<td>73.1%</td>
<td>27.8%</td>
<td>25.9%</td>
</tr>
<tr>
<td>MVV (percent predicted)</td>
<td>57%</td>
<td>20%</td>
<td>21%</td>
</tr>
<tr>
<td>RV (liters)</td>
<td>2.7</td>
<td>4.3</td>
<td>4.2</td>
</tr>
<tr>
<td>TLC (liters)</td>
<td>5.7</td>
<td>6.6</td>
<td>6.4</td>
</tr>
<tr>
<td>7 Minute Nitrogen Washout &gt;2.5%</td>
<td>0</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>PaO2 (mm Hg)</td>
<td>71.2</td>
<td>56.8</td>
<td>49</td>
</tr>
<tr>
<td>PaCO2 (mm Hg)</td>
<td>35</td>
<td>39</td>
<td>53.6</td>
</tr>
<tr>
<td>pH</td>
<td>7.40</td>
<td>7.44</td>
<td>7.39</td>
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</tbody>
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**FIGURE 1.** Blood gas changes with ultrasonic/air and IPPB/ultrasonic/air in a group of ten control patients.
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symptoms and only three had a drop in PaO2.

The patients with COLD, ie groups 2 and 3, interrupted treatment four out of 15 times with U/air but seven out of ten times with IPPB/U/air. Interruption of inhalation therapy was for coughing, shortness of breath, choking, or fatigue and consisted of one to five brief episodes. These interruptions undoubtedly tended to allow restoration of blood gas abnormalities and reduced the degree and frequency of abnormalities.

Group 1 control patients tolerated ten separate treatment periods of 20 minutes each of U/air and IPPB/U/air therapy without interruption except for one episode, despite a significant drop in PaO2 during seven of the treatment periods.

In a separate study of four patients, four liters per minute nasal oxygen was administered along with ultrasonic therapy. PaO2 rose an average of 70 mm from the baseline with the PaO2 ranging from 97.7 to 168 mm Hg during therapy. Three of the four patients had fewer symptoms with oxygen (U/O2) than with U/air.

shows a significant rise in PaCO2, but three in group 1 and four in group 2 showed significant reductions. As expected, the serum pH reflected these changes, and five patients had a rise in pH of 7.5 or higher. Two were from group 1, one of whom developed a pH of 7.6. Three of these patients were from group 2, one of whom had a pH rise to 7.63 (Fig 6), which was associated with a 15 mm decline in PaO2. None of the patients with baseline hypercapnia (group 3) showed any significant change in serum pH or PaCO2.

Symptoms of shortness of breath, headache, choking sensation, and chest pain occurred in ten of 15 patients with COLD treated with U/air, and of these, seven (70 percent) had a significant drop in PaO2. However, two of the five patients who did not complain of symptoms also had a drop in PaO2. None of the patients in the control group complained of U/air therapy, yet all of the five patients had a drop in PaO2. All ten COLD patients treated with IPPB/U/air complained of symptoms and only three had a drop in PaO2.
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Previously reported by Pflug and co-workers of a decline in PaO₂ in a substantial percentage of COLD patients treated with ultrasonic nebulization, although different nebulization methods were used. We used normal saline, which may have caused a greater increase in airway resistance than the 0.45 normal saline solution used by Pflug and colleagues, but we also used a face tent rather than mouthpiece. Further evidence that symptoms in our COLD patients were due to an increase in airway resistance is the observation that our control patients had no symptoms, but they showed similar, if not even greater, declines in PaO₂. In addition, increase in bronchial airway resistance was not observed by Cheney and Butler in their control patients and only in one of eight normals exposed to artificial fog by Abernethy. Furthermore, symptoms and blood gas changes in our study did not coincide consistently in COLD patients, especially when IPPB was added to ultrasonic therapy.

FIGURE 4. Patient 1, group 3. With U/air the decline in PaO₂ is associated with a rise in PacO₂ and a decline in pH to 7.32. These changes suggest hypoventilation as the cause for the increase in hypoxia and occurred despite interruptions of treatment twice. These changes were not seen with IPPB/U/Air.

FIGURE 5. Patient 1, group 2. Hyperventilation is induced by both U/air and IPPB/U/air. Complaints were present, however, only with IPPB/U/air and resulted in the patient's interrupting treatment three times. Note that the decline in PacO₂ with U/air is associated with an initial rise in PaO₂ to 9 mm Hg above the baseline. Note that the pH rose to 7.63 with both forms of treatment.

DISCUSSION

Objective evaluation of the clinical value of inhalation therapy is difficult. A recent editorial succinctly described the dilemma of the increasing popularity of IPPB inhalational therapy despite conflicting favorable and unfavorable data for both physiologic and clinical studies following treatment. The same holds with the introduction of ultrasonic therapy. Wolfsdorf and associates utilizing labelled water calculated that at the most 80 milliliters per 24 hours was deposited in the lower respiratory tract through use of direct mouth tube breathing and far less through use of the face hood technique or tent. Ten or 20 minutes of treatment would indeed represent a very small quantity.

In addition, several studies clearly indicate that ultrasonic treatment produces an increase in bronchial airway resistance in patients with COLD or reactive bronchial trees. This is reversible with bronchodilator therapy and is felt to be mainly bronchoconstrictive in nature. This could best explain the symptoms of choking, shortness of breath, and tightness of the chest which are so common. Our blood gas studies confirmed the findings previously reported by Pflug and co-workers of a decline in PaO₂ in a substantial percentage of COLD patients treated with ultrasonic nebulization, although different nebulization methods were used. We used normal saline, which may have caused a greater increase in airway resistance than the 0.45 normal saline solution used by Pflug and colleagues, but we also used a face tent rather than mouthpiece. Further evidence that symptoms in our COLD patients were due to an increase in airway resistance is the observation that our control patients had no symptoms, but they showed similar, if not even greater, declines in PaO₂. In addition, increase in bronchial airway resistance was not observed by Cheney and Butler in their control patients and only in one of eight normals exposed to artificial fog by Abernethy. Furthermore, symptoms and blood gas changes in our study did not coincide consistently in COLD patients, especially when IPPB was added to ultrasonic therapy.

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coughing which is usually induced undoubtedly adds to the workload also. The addition of IPPB to ultrasonic treatment presumably should have resulted in a reduction of workload of breathing. Indeed, PaO₂ was higher on the average with IPPB/U/air. However, this was the result of increased ventilation as shown by the mean decrease in Paco₂ and rise in pH. In those who had a decreased PaO₂ there was a higher incidence of unaltered or depressed Paco₂, again implying altered ventilation-perfusion relationships as the major mechanism.

Acute blood gas changes, such as hypoxia, respiratory acidosis, and especially respiratory alkalosis, carry the potential of triggering serious cardiac arrhythmias. In the past year we have seen two patients who had cardiac arrest during IPPB/U/O₂ therapy, which was being given as part of postoperative care. Bronchodilator drugs were not being administered in these two patients. Postmortem examination revealed moderately severe coronary atherosclerosis without myocardial infarction in one. In the other an autopsy was not obtained, but during resuscitative efforts ECG changes consistent with acute myocardial infarction were noted. The role inhalational therapy played in triggering the terminal episodes is speculative at the present.

Physicians who observe inhalational therapy being given to their patients or experience it themselves best appreciate why some patients have difficulty and discomfort. This is particularly true with IPPB/U. IPPB is most logically indicated in hypoventilating COLD patients but is most likely to cause discomfort in this very group. For technicians to struggle with patients and insist that they continue on inhalational therapy when they feel uncomfortable is probably hazardous. An overzealous physician or technician may indeed endanger a patient's life. Clinically, inhalational therapy seems to be useful in selected cases mainly in inducing production and expectoration of sputa, whether this is due to actual increased delivery of moisture to the lower bronchial tree or not. Before routine usage, one should consider the known hazards of nosocomial infections, as well as the effects on airway resistance and the blood gas changes. The airway resistance can be reversed by adding bronchodilators, and hypoxia by giving oxygen. However, other acute blood gas changes, such as respiratory alkalosis and respiratory acidosis may still occur.

Despite the 67 percent incidence of complaints of discomfort with ultrasonic nebulization, the curious paradox is that the majority of patients under direct questioning felt that the treatment was "beneficial." This subjective improvement was judged by feel-
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ings of posttreatment improvement of breathing and easier expectoration of sputa. This was equally true of those who had ultrasonic delivered by IPPB, in whom the incidence of discomfort was even higher. How much of the improvement was real and how much the influence of exposure to impressive and uncomfortable treatment is difficult to assess objectively.

REFERENCES
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5 Sputum inducement—aerosol vs bronchial lavage, in Proceedings of the First Conference on Clinical Applications of the Ultrasonic Nebulizer 1966, pp 49-50

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Trials and Tribulations of a Pioneer Anatomist

Andreas Vesalius (1514-1564), a man of German extraction, a teacher at Padua, was the first true anatomist. He recorded what he saw not what authority said he should see. The fruit of his work is the great DE FABRICA HUMANI CORPORIS, published in 1543. The response was immediate and violent. By some he was tolerantly ignored, others openly derided him, some used the authorities to impose upon him petty persecutions. In indignation Vesalius, then barely thirty, burned his manuscripts, retired from anatomy, and became physician to Emperor Charles V. Vesalius in retirement was being forgotten. In 1563, he went on a pilgrimage to Jerusalem. On his way back, he received word that he was to have back his old position at Padua. But he was never to realize the ambition that had cankered him so since the day he had become a courtier. On the journey home he sickened and died.

Haggard H W: Mystery, Magic and Medicine. Garden City, N Y, Doubleday, Doran, 1933