Inhalation of Varying Concentrations of Oxygen in the Treatment of Severe Pulmonary Insufficiency*

DOUGLAS DAVID, M.D.,** ROBERT M. POSKE, M.D.,
and ANGELO TOIGO, M.D.
Hines, Illinois

Acute pulmonary insufficiency in chronic pulmonary disease is a medical emergency. Its therapy is difficult, and the mortality is great. A number of approaches to the problem have been employed, including the use of antibiotics, corticosteroids, oxygen, tracheotomy, and various mechanical devices to improve respiration. The physiologic derangement seen in this condition is relatively constant although it may occur in a wide variety of diseases. There is severe arterial hypoxia and hypercapnia. Associated with the persistent hypercapnia is a decreased sensitivity of the respiratory center to the stimulus of carbon dioxide. The sole remaining stimulus to respiration is the hypoxia. When the arterial oxygen is increased above physiologic levels, such as occurs during breathing of 100 per cent oxygen, this stimulus is lost, alveolar ventilation decreases, arterial hypercapnia increases, the pH of the arterial blood decreases, and death ensues.

In order to decrease the hypercapnia or minimize its increase and, at the same time, prevent severe hypoxia, oxygen in concentrations of less than 100 per cent was used in the treatment of this condition. The sensitivity of the medullary respiratory center to $F_{CO_2}$ may thus be gradually increased. What role the increased arterial oxygen plays in this improvement is unknown. The observations obtained from this form of therapy are the subject of this report.

Methods

All patients evaluated had chronic pulmonary disease, but of different etiologies. They were acutely ill with severe pulmonary insufficiency at the time of these observations.

Studies were performed with the patients breathing ambient air, 100 per cent of oxygen by nasal catheter, and varying concentrations of oxygen administered by IPPB/I (intermittent positive pressure breathing, inspiratory). Arterial blood samples were obtained and analyzed for oxygen and carbon dioxide tensions by the Riley bubble technique. Admittedly, this is not the most accurate procedure available, but with a well-trained biochemist, periodically checked by tonometer studies, the physician at the bedside can quickly obtain valuable clinical information which will give an objective approach to further treatment. Varying concentrations of inspired oxygen were obtained by mixing compressed air and 100 per cent oxygen in the nebulizer of a Bennett Model PR-1A Respirator.

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*From the Cardiopulmonary Laboratory and the Medical Service, Veterans Administration Hospital, Hines, Illinois.
**Director, Cardiopulmonary Laboratory, Saint Joseph Infirmary, Louisville, Kentucky.
Results

Table 1 illustrates the role of varying the concentrations of oxygen in the treatment of these emergency problems. Some of the data presented concern the early cases for which equipment was not yet available to deliver the necessary low-oxygen concentrations. These patients (Table 1, cases R.M.W., A.T.F., and G.C.) did not do well physiologically although some of them did improve clinically.

One of us (D.D.) then improvised a method of mixing compressed air with 100 per cent oxygen in the IPPB/I apparatus in order to secure the desired concentrations of oxygen for inhalation. The most effective levels of inspired oxygen in these patients were found to lie between 25 and 35 per cent with 12 centimeters of water pressure. The physiologic improvement in these cases, as shown by arterial oxygen and carbon dioxide tensions, was paralleled by clinical improvement. As may be seen in the case of A.F., the breathing of either mixture under pressure relieved the hypoxemia, but the breathing of 32 per cent O₂ was associated with a higher arterial CO₂ tension than was the breathing of 27 per cent O₂. In view of the effects of respiratory acidosis and the increased prospect of narcosis and coma as a complication of arterial hypercapnia, one should choose the inspired oxygen concentration which raises the arterial O₂ tension within physiological limits. This must be done, however, without increasing the hypercapnia and possibly decreasing it. Clinically, in these

<table>
<thead>
<tr>
<th>Patient</th>
<th>Before Trial Therapy</th>
<th>Method of Oxygen Administration</th>
<th>After Trial Therapy</th>
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<tbody>
<tr>
<td></td>
<td>P₀₂*</td>
<td>Fₐ₃*</td>
<td>P₀₂*</td>
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<tr>
<td></td>
<td>Per cent Oxygen (Approximate)</td>
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<td>Fₐ₃*</td>
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<tr>
<td>R.M.W.</td>
<td>39</td>
<td>IPPB/I 20 minutes, 12 cm.H₂O</td>
<td>118</td>
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<td>62</td>
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<td>76</td>
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<tr>
<td>A.T.F.</td>
<td>26</td>
<td>IPPB/I 12 minutes, 12 cm.H₂O</td>
<td>108</td>
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<td>77</td>
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<td>93</td>
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<td>G.C.</td>
<td>68</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
<td>252</td>
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<td>83</td>
<td></td>
<td>97</td>
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<tr>
<td>J. A.</td>
<td>22</td>
<td>IPPB/I 15 minutes, 18 cm.H₂O</td>
<td>64</td>
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<tr>
<td></td>
<td>73</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
<td>76</td>
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<tr>
<td></td>
<td>100</td>
<td>Nasal catheter 1 hour, 8 liters per minute</td>
<td>49</td>
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<td></td>
<td>80</td>
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<td>M.K.</td>
<td>27</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
<td>150</td>
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<td></td>
<td>59</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
<td>116</td>
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<td></td>
<td>35</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
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<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
<td>116</td>
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<td></td>
<td>100</td>
<td>Nasal catheter 15 minutes, 5 liters per minute</td>
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<td></td>
<td></td>
<td>63</td>
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<tr>
<td>R.W.</td>
<td>51</td>
<td>IPPB/I 10 minutes, 12 cm.H₂O</td>
<td>45</td>
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<td>74</td>
<td>IPPB/I 10 minutes, 12 cm.H₂O</td>
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<tr>
<td>A.F.</td>
<td>32</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
<td>154</td>
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<td></td>
<td>77</td>
<td>IPPB/I 15 minutes, 12 cm.H₂O</td>
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* Arterial oxygen and carbon dioxide tensions in millimeters of mercury.

† Manufactured by Bennett Respiration Products, Inc.
patients there seems to be an increase in tidal volume and a decrease in the work performed during respiration when IPPB/I is initiated.

It is interesting to note that in the case of M.K., despite the arterial oxygen tension 27 mm. Hg., the arterial carbon dioxide tension was only 59 mm. Hg. while breathing ambient air. This case, in contrast to case J.A., reveals how a relatively small increment in inspiratory $O_2$ concentration under pressure increased the arterial oxygen tension above the normal physiological limits. As will be brought out later, the patient's response to a given inspired oxygen concentration is dependent on his underlying respiratory defect.

**Discussion**

It should be emphasized that all of these patients were acutely ill, and oxygen therapy was therefore supplemented by other means of improving alveolar ventilation such as the employment of bronchodilators, antibiotics, corticosteroids, expectorants, etc. It is not the purpose of this paper to review or evaluate the numerous therapeutic agents or procedures that are utilized in the treatment of severe pulmonary insufficiency, but to demonstrate and discuss the physiologic basis for the use of oxygen.

Our studies tend to confirm the documented observation that relief of arterial hypoxemia with physiologic levels of arterial oxygen has little effect on minute ventilation in patients with pulmonary emphysema and carbon dioxide retention. However, a considerable increase in arterial $P_{O_2}$ such as occurs with breathing 100 per cent oxygen, elicits a marked decrease in minute ventilation. This suggests that it is important to distinguish between physiologic and pathophysiologic levels of oxygen tension in the arterial blood.

We have also shown that it is not necessary to leave a patient severely hypoxic because of fear of apnea or alveolar hypoventilation. Because of economic reasons, we have chosen to vary the inspired oxygen concentration by diluting 100 per cent oxygen with compressed air (there is clinical evidence that helium-oxygen mixtures are effective in acute pulmonary insufficiency, but the expense involved precludes their routine use).

The increase in arterial oxygen tensions to a given inspired concentration of oxygen will depend on the underlying pulmonary structural pathology present; consequently, no two patients will respond exactly alike. This is important physiologically because it emphasizes the necessity of varying the concentration of inspired oxygen and of subsequently obtaining arterial samples in order to reach the point, in each patient, at which the area of oxygenation is within the physiologic range and the carbon dioxide has minimally increased or has decreased. Of course, the response to a given inspired oxygen concentration may change as is occasionally suggested by lack of clinical improvement. In such situation it will be necessary to repeat the arterial puncture in 12 to 24 hours.

Usually, our patients were withdrawn from IPPB/I in 36 to 96 hours. This depended on the reversibility of the acute stress on the limited pulmonary reserve and on the complications secondary to hypoxia. Patients have not only shown a change in the level of consciousness after treatment, but also changes in personality.

The effects of pressure breathing on ventilation and circulation have been reported by many investigators. Numerous mechanical devices have been used in a variety of ventilatory disorders. The positive pressure applied to the patients with chronic pulmonary insufficiency during IPPB/I inflates the lung to a greater extent than during normal inspiration, thereby providing better alveolar ventilation and a more uniform distribution. However, it should be stressed that this therapy may produce unwanted changes in cardiopulmonary dynamics. It should also be pointed out that without controlled respiration (such as with the use of succinylcholine) the use of respiratory body chambers (Emerson and Drinker types) in patients with obstructive pulmonary emphysema may further decrease the arterial $P_{O_2}$ and increase the arterial $P_{CO_2}$. This is probably due to the increased work of breathing and the associated alveolar hyperventilation caused when the patient "ights" the respirator.

We have used the nasal catheter humidification technique employing different oxygen flows to obtain the arterial oxygen tension desired. However, this method has not always been physiologically or clinically successful. We have seen tachypneic patients respond to IPPB/I whose arterial oxygen tensions were not in the physiologic range because low oxygen flows through a nasal catheter. The danger of low oxygen flows (1 to 2 liters per minute) through a nasal catheter in patients with acute pulmonary insufficiency is the persistence of severe hypoxia. This state may go unrecognized if arterial gas tensions are not determined.
SUMMARY

1. The management of the hypoxemia of acute pulmonary insufficiency in chronic lung disease is often a difficult emergency problem.

2. Ideally, oxygen should be administered in this condition in such a way as to increase the arterial oxygen tension without aggravating the hypercapnia.

3. The choice of oxygen therapy will therefore depend on the response of the patient's arterial gas tensions to a given inspired oxygen concentration however delivered. This response will vary from patient to patient according to the pulmonary structural pathology present.

4. The importance of determining arterial gas tensions initially and after each variation in oxygen therapy is stressed. Repeated determinations in 12 to 24 hours may be indicated if clinical improvement does not occur.

5. Oxygen administered by the nasal catheter humidification technique may not be adequate. Low oxygen flows given by this method may actually prolong the hypoxemia state.

6. A method is described in which varying oxygen concentrations were effectively employed in the IPPB/I (intermittent positive pressure, inspiratory) apparatus.

ADDENDUM: Since this article was submitted for publication, one of the authors (D.D.) has worked with Bennett Respiration Products, Inc. to produce a simplified and more physiologic method of delivering varying concentrations of inspired oxygen between 20 and 40 per cent. We have also incorporated into the machine nebulization on inspiration only. Below is a brief description of the apparatus that we have been using.

A Bennett pedestial IPPB Therapy Unit (Model PV-3P), with the air diluter modified to give approximately 35 per cent oxygen concentration when 100 per cent oxygen is used as the source gas. It is equipped with continuous and intermittent nebulizer needle valves, and served by two Puritan regulators with nebulizer needle valves and pressure compensated flowmeters, one calibrated for oxygen, the other for air, manifolded to a single outlet.

RESUMEN

1. El manejo de la hipoxemia en la insuficiencia pulmonar aguda en la enfermedad pulmonar crónica es a menudo una emergencia difícil de resolver.

2. Idealmente el oxígeno debe ser administrado en estas condiciones de tal manera que aumente la tensión arterial del oxígeno sin agravar la hiperkapnia.

3. La elección de la oxigenoterapia dependerá por tanto de la respuesta de las tensiones de gas arterial en los enfermos a una concentración dada de oxígeno. Esta respuesta será diferente de un enfermo a otro de acuerdo con la estructura patológica presente.

4. La importancia de determinar las tensiones de gas arterial inicialmente y después de cada variación en el tratamiento con oxígeno se hace resaltar. Las determinaciones repetidas en 12 a 24 horas pueden indicar si la mejora clínica no ocurre.

5. La administración de oxígeno por el cateter nasal con humidificación puede no ser adecuada. El flujo del oxígeno dado por esta técnica puede de hecho prolongar el estado hipóxico.

6. Se describe un método en el que se emplearon concentraciones variadas de oxígeno con resultados efectivos con el aparato de presión intermitente positiva inspiratoria (IPPB/I).

RESUMÉ

1. La conduite thérapeutique de l'hypoxémie de l'insuffisance pulmonaire aiguë dans les maladies pulmonaires chroniques est souvent un problème d'urgence difficile.

2. Idéalement, l'oxygène devrait être administré dans cet état de telle sorte qu'on obtienne l'augmentation de la teneur oxygénée artérielle sans aggraver l'hypercapnée.

3. Le choix de la thérapeutique oxygénée dépendra alors de l'importance de la tension des gaz artériels du malade à une concentration donnée de l'oxygène inspiré. Cette réponse variera d'un malade à l'autre selon l'état pathologique de ses poumons.

4. L'auteur met l'accent sur l'importance qu'il y a à déterminer les tensions des gaz artériels au début et après chaque modification de la thérapeutique oxygénée. Des examens répétés toutes les douze ou 24 heures peuvent être nécessaires si l'amélioration clinique ne survient pas.

5. L'oxygène administré par la méthode d'humidification du cathéter nasal peut ne pas être convenable. Des taux faibles d'oxygène administrés par cette méthode peuvent prolonger l'état hypoxique.

6. L'auteur décrit une méthode dans laquelle des concentrations diverses d'oxygène sont effectivement utilisées dans un appareil à pression positive intermittente, inspiratoire.
ZUSAMMENFASSUNG

1. Die Behandlung der Hypoxie bei der akuten pulmonalen Insuffizienz während chronischer Lungenerkrankung ist oft ein schwieriges Problem akuter Dringlichkeit.

2. Im Idealfall sollte man Sauerstoff in einem solchen Zustand in der Weise geben, daß die arterielle Sauerstoff-spannung ansteigt, ohne daß die Kohlensäuregehalten des Blutes übermässig zunimmt.


6. Es wird eine Methode beschrieben, bei der verschiedene Sauerstoffkonzentrationen in dem Gerät für intermittierende positive Druckatmung in wirksamer Weise zur Anwendung gelangte.

REFERENCES


ELECTROCARDIOGRAPHIC CHANGES IN DOGS DUE TO HYPOXIA

Changes in the electrocardiographic pattern induced by experimental hypoxia (7 per cent in O₂ in N₂) in a group of 13 dogs are described. During hypoxia, in most of the dogs, an increase to the positive potential of the T wave and of the Q-T time has been observed. These findings would indicate that hypoxia causes, in the dog, a lengthening of the "activation" time of the subendocardial layers of the myocardium, in contrast with the phenomena that take place under comparable conditions in normal human subjects and in patients with coronary disease.