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Continuous or Nocturnal Oxygen Therapy in Hypoxemic Chronic Obstructive Lung Disease

A Clinical Trial

NOCTURNAL OXYGEN THERAPY TRIAL GROUP*

At six centers, 203 patients with hypoxemic chronic obstructive lung disease were randomly allocated to either continuous oxygen (O_2) therapy or 12-hour nocturnal O_2 therapy and followed for at least 12 months (mean, 19.3 months). The two groups were initially well matched in terms of physiological and neuropsychological function. Compliance with each oxygen regimen was good. Overall mortality in the nocturnal O_2 therapy group was 1.94 times that in the continuous O_2 therapy group ($P = 0.01$). This trend was striking in patients with carbon dioxide retention and also present in patients with relatively poor lung function, low mean nocturnal oxygen saturation, more severe brain dysfunction, and prominent mood disturbances. Continuous O_2 therapy also appeared to benefit patients with low mean pulmonary artery pressure and pulmonary vascular resistance and those with relatively well-preserved exercise capacity. We conclude that in hypoxemic chronic obstructive lung disease, continuous O_2 therapy is associated with a lower mortality than is nocturnal O_2 therapy. The reason for this difference is not clear.

PATIENTS WITH chronic obstructive lung disease and hypoxemia have a poor prognosis in spite of treatment regimens aimed at improving the mechanical function of the lungs (1). Because of this, such patients are often treated with supplementary oxygen on an outpatient basis. Early studies of this treatment, which compared patients before and after oxygen therapy, indicated that chronic O_2 therapy resulted in improved exercise tolerance, decreased pulmonary hypertension and erythrocytosis, and improved neuropsychological function (2-6). A trial in which oxygen was given to one group of patients but withheld from a similar control group has not been done in North America, but such a trial is underway in the United Kingdom, and a preliminary report indicates that oxygen administration was associated with a reduced mortality (7).

Long-term oxygen administration is an expensive form of treatment, particularly when ambulatory patients are supplied with portable units. It is not clear whether continuous O_2 therapy is necessary; patients suffer their most severe hypoxemia while sleeping (8), and it is possible that hypoxemic sequelae such as erythrocytosis and pulmonary hypertension could be prevented by exclusively nocturnal oxygen administration. Indeed, there is some evidence that pulmonary hypertension can be reduced by as little as 15 hours of oxygen administration per day (9, 10).

On the basis of this rationale, the Division of Lung Diseases of the National Heart, Lung, and Blood Institute initiated a multicenter clinical trial comparing continuous O_2 therapy with nocturnal O_2 therapy in patients with hypoxemic chronic obstructive lung disease (11).

Methods

The protocol for the trial has been published elsewhere in detail (12) and therefore will be presented briefly here. Six treatment centers recruited 203 patients over 27 months and followed each surviving patient at least 1 year. The number of patients at each center varied from 26 to 44. Entry and exclusion criteria are shown in Table 1. The most important entry criterion was, of course, hypoxemia. The protocol required that this criterion be fulfilled on at least two occasions more than 1 week apart during a 3-week observation period while the subject was free of exacerbations and was managed without supplemental oxygen and with intensive bronchodilator therapy. In practice, patients were initially identified as fitting the entry but not the exclusion criteria, recruited in a preliminary way, and observed for 3 weeks to ensure stability. At the end of this time, if the patients still met these criteria, informed consent was obtained and the patient was hospitalized for a week of baseline studies. At the end of these studies, each patient was randomly allocated by the Data Center to either continuous O_2 or nocturnal O_2 therapy. Randomization schedules were developed sepa-

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