Brain Dysfunction in COPD

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Clinicians have long recognized that patients with far advanced COPD can develop intellectual impairment or delirium as a correlate of severe hypoxemia or hypercapnia. At the same time, there have been no systematic studies of cerebral functioning in the person with hypoxic COPD who is still able to continue functioning on an ambulatory basis (with or without oxygen supplementation). We do not know the extent to which brain functions in such patients might slowly and subtly decline, thereby contributing to the behavioral picture of erasability, inflexibility, depression and non-compliance with treatment that seem to be commonplace among COPD patients. In the present report we will describe some preliminary observations of neuropsychologic status gathered from 121 hypoxemic COPD patients as part of the Nocturnal Oxygen Therapy Trial (NOTT).

METHODS AND MATERIALS

NOTT is a multicenter clinical trial designed to assess the comparative effectiveness of nocturnal (12 hour) and continuous (20 hour or more) oxygen treatment in patients with hypoxic COPD. Before entering treatment, all patients received baseline medical, neuropsychologic, and psychosocial evaluations. This report presents baseline neuropsychologic findings prior to an extended oxygen therapy program.

Subjects

There were 121 patients (80 percent men and 20 percent women). Their demographic characteristics were: age 65.1 ± 8.6; race, 81 percent white, 18 percent black, 1 percent other; education, 31 percent high school or above, 20 percent grades 10 or 11, 31 percent grades 7-9, 18 percent below 7 years of formal education.

Baseline physiologic characteristics were: PaO₂, 51.2 ± 5.3 mm Hg; PaCO₂, 43.3 ± 7.8 mm Hg; bicarbonate, 30.2 ± 5.8 mEq/L; hematocrit 48.1 ± 5.4 percent; FVC 1.950 ± 0.710 L; FEV₁, 0.740 ± 0.341 L; PVR 366.1 ± 190.1 dynes-cm sec⁻²; PAP 29.5 ± 10.8 mm Hg; cardiac index 2.89 ± 0.63 L min⁻¹/m²; max work (room air) 39.7 ± 17.3 watts.

Neuropsychologic Assessments

Neuropsychologic tests are measures of abilities whose deterioration generally reflects disturbance in physiologic or structural integrity of the brain. The specific methods used here have been termed the Halstead-Rrian neuropsychologic test battery. Changes in performance on this battery have been shown to correlate well with neurologic criteria. Each patient's entire set of neuropsychologic (NP) results was reviewed independently by two clinicians (IG and RKH). The clinicians grouped tests according to the mental abilities which they primarily reflected: attention, language, abstracting ability (conceptual thinking), sensation (simple perceptual skills), simple motor skills, perceptual-motor integration (problem solving and other complex skills), and memory (30 minute recall of verbal and nonverbal information). Each ability was scored on a 6-point scale from "excellent" to "severely impaired." The clinicians also assigned a composite score of 1 through 6 to summarize their overall impression of each patient's NP status.

RESULTS

The NP findings are presented in Figure 1. Most patients had disturbances in abstracting ability (79 percent) and complex perceptual motor integrative abilities (84 percent). Deficits in simple motor skills and attention were the next most common, whereas language and memory were generally intact. Each bar in the histogram (Fig 1) has three types of shading to permit the reader to observe what proportion of patients had mild, moderate, or severe deficit for the ability in question. Taking all NP information into account, the clinicians classified only 23 percent of patients normal and 37 percent of the patients mildly, 29 percent moderately and 11 percent severely impaired (Fig 1).

There were few significant correlations between overall NP status and physiologic variables. The product moment correlation between the neuropsychologists' global judgment and PaO₂ was -0.34 (P < .001) and between NP and maximum work achieved on room air (treadmill) was -0.19 (P < .05). There were no associations between NP and hematocrit, PaCO₂, pH, dynamic and static spirometry, or hemodynamic studies, with the exception that FEV₁ postbronchodilator correlated with NP rating at r = -0.26 (P < .02).

CONCLUSIONS

Many ambulatory patients with moderately advanced COPD have neuropsychologic deficits suggestive of organic brain dysfunction. In general, the highest cogni-
tive functions (reasoning, perceptual-motor integration) are most severely affected, although memory appears to be relatively spared. About half the patients had definite motor difficulties, while verbal skills tended to be preserved.

We do not have adequate data to speculate on which physiologic changes attendant to COPD are contributing to CNS disturbance. The negative correlation with arterial oxygenation is impressive considering the narrow range of arterial oxygen levels imposed by the patient selection criteria of $\text{PaO}_2 \leq 59 \text{ mg Hg}$. Although treatment effects have not yet been considered in the present study, the relationships between hypoxemia and neuropsychologic functioning in our patients are consistent with earlier reports that oxygen treatment may improve mental abilities\(^2\) and EEGs\(^3\) in selected COPD patients.

As the NOTT patients receive repeat evaluation at the completion of six months of oxygen treatment, we should be in a better position to determine whether cerebral function improves or if there is evidence of persisting organicity despite systematic correction of hypoxemia. Of more immediate significance to the physician, our results underscore that for many patients, hypoxic COPD is associated with disease of the brain as well as of the lungs and heart.

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REFERENCES


Q. (Martin): Do patients know that they are impaired?

A. (Grant): People vary in ability to assess how they function. Depressed people vary a lot in their response and frequently are not correct in their impression.

Q: What is your control group—normals or patients with COPD?

A. (Grant): Non-COPD patients. Lack of a adequate untreated control group does present a problem in this study.

Q. (Loudon): Do some of the drugs used for pulmonary patients have an effect on psychologic testing?

A. (Grant): Drugs used were not entirely controlled. Some of the drugs used do have an antidepressive effect.

Q: Do you agree that an untreated COPD group should be used as controls?

A. (Grant): Yes, but this is not possible in the current study since we are comparing different types of oxygen therapy and not therapy with therapy.

**Chronic Obstructive Pulmonary Disease; Socioemotional Adjustment and Life Quality**

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Clinical reports and previous studies have suggested that COPD patients experience negative changes in mood and social behavior similar to those found in studies of chronic hypoxia.\(^1\)-\(^3\) Unfortunately, a truly comprehensive assessment of the effects of COPD on emotional functioning, social adjustment and related aspects of life quality does not yet exist. In light of this fact, the investigators in the Nocturnal Oxygen Therapy Trials (NOTT) agreed that a comprehensive assessment of life quality would be appropriate and indeed crucial in the evaluation of oxygen therapy.

**Methods**

**Patient Population**

Subjects for the study are 166 patients enrolled in the Nocturnal Oxygen Therapy Trials, a multi-side study designed to compare the effectiveness of Nocturnal and Continuous Oxygen Therapy with patients who have severe COPD. Eighty percent of the patients are men, 20 percent women. The mean age of the sample is 65.6 (SD = 8.6); 98 percent are past and/or current smokers. Mean $\text{Pao}_2$ at entry is 50.1 (SD = 5.1). Additional information concerning the patient sample is available in Grant et al.\(^4\)

**Assessment Procedures**

Our working definition of life-quality encompasses four basic dimensions: a) emotional functioning, including mood changes and other psychiatric symptoms; b) social role functioning, including employment, home management, and social and family relationships; c) basic behavioral functioning, including self-care skills and mobility; and d) ability to engage in enjoyable hobbies and recreational pastimes.

To measure these aspects of life quality, we first chose three standard self-report measures: The Minnesota Multiphasic Personality Inventory (MMPI),\(^5\) the Profile of Mood States (POMS)\(^6\) and the Sickness Impact Profile (SIP).\(^6\) The MMPI assesses emotional adjustment and psychiatric disturbance, the POMS serves as a measure of current mood and the SIP measures 12 categories of physical and psychosocial activities that are likely to be affected by illness.

The MMPI, POMS and SIP are supplemented by two additional measures that allow us to assess the patient's function from the perspective of others: The Katz Adjustment Scale (KAS)\(^5\) and the Home Visit Behavior Checklist (HVBC). The KAS is a standard measure of social adjust-

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