Q: Can you more precisely define your patients with COPD?
A. (Cutillo:) We used the above mentioned physiologic criteria to define our patients. We purposefully excluded patients with asthma.

Elastic and Resistive Loading in Chronic Obstructive Lung Disease*

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Respiratory neuromuscular output as measured by the mouth occlusion pressure increases in normal subjects when the resistance to airflow is heightened acutely.

In studies conducted by Altose et al in patients with chronic obstructive lung disease, the compensatory response to resistive loading was found to be significantly blunted.

The diminished occlusion pressure response to flow loading in patients with chronic obstructive lung disease could be due to inspiratory muscle weakness or muscle fatigue. Alternatively, abnormalities in the function of proprioceptive receptors in the muscles of the thoracic cage or in vagal mechanoreceptors in the lung or their central processing could explain the abnormal response to external flow loading.

It was reasoned that defective respiratory muscle function should affect the occlusion pressure response to both types of loads equally. If impairment of sensory mechanisms accounted for the blunted P100 response to flow loads in COPD the response to an elastic load need not be affected. To further evaluate these possibilities, we compared the effects of elastic and inspiratory flow resistive loads on ventilation and occlusion pressure in patients with COPD.

METHODS

We studied 14 patients with COPD and seven age-matched normal subjects. All were in a stable clinical and functional state at the time of study. Mean age was 56 ± 1.7 SE; mean FEV1, 43 percent ± 3.5 SE of predicted value. All had symptoms of cough and/or dyspnea and radiologic evidence of hyperinflation.

Progressive hypercapnia was produced by having seated subjects rebreathe a gas mixture of 7 percent CO2 in oxygen. One hundred percent oxygen was breathed for four minutes prior to rebreathing to prevent changes in hypoxic drive during the rebreath. End tidal CO2 concentrations were measured with an infrared analyzer (Beckman). Tidal volumes were recorded by electrical integration of the signal from a pneumotachograph (Fleisch 2, i/a 7320) with a Statham differential pressure transducer (PM-5, Statham Instruments Division, Gould, Inc., Calif.).

Mouth occlusion pressure was measured 100 msec after the

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Figure 1. P100 response to flow resistive and elastic loading in a representative COPD patient. Data were obtained during free rebreathing (†), with an inspiratory resistance of 18 cmH2O/L/sec (O) and with an elastic load of 19 cmH2O/L (X). Occlusion pressure values obtained at the mouth 100 msec after an occluded inspiration are shown on the vertical axis.

onset of inspiratory effort following airway occlusion P100 and eight to ten occlusions were performed randomly during each rebreathing trial. Elastic loading of 19 cm/L was achieved by enclosing the rebreathing bag in a rigid container (14 gallon). To maintain a constant load, the container was vented by a Satt valve. Flow resistive loading was performed by placing wire mesh screens (18 cmH2O/L/sec) on the inspiratory side of the circuit.

Minute ventilation was calculated from the three breaths preceding the occluded breath. Ventilatory and occlusion pressure responses to CO2 were determined from the slope of the regression lines calculated by the method of least squares.

RESULTS

Both elastic and flow resistive loading altered the pattern of breathing in normal subjects.

Patients with COPD and normal subjects had a similar breathing pattern on elastic loads. There was always a decrease in VT and a compensatory increase in breathing frequency. In the patient and control groups breathing patterns were not consistent on flow loads. In the COPD patients, the ventilatory response to hypercapnia (∆Ve/ ∆Pco2) was significantly lower in the unloaded, as well as in both loaded situations than in the normal group.

In normal subjects, the occlusion pressure response to hypercapnia increased significantly during both flow resistive and elastic loading from 0.47 ± SE.04 (control) to 0.66 ± SE.05 (resistive) and 0.93 ± SE.11 (elastic).

The average occlusion pressure in the patient group on the elastic load was 190.7 percent ± SE 24 of the control value which was indistinguishable from the response of normal subjects to the elastic load. The occlusion pressure response to flow loading was unchanged by the resistive load (Fig 1).

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DISCUSSION

The normal occlusion pressure response to elastic loads in COPD patients in whom the response to flow loads is impaired indicates that the diminished response to flow loads cannot be explained by decreased muscle performance or fatigue. Rather, this phenomenon appears to represent a specific defect perhaps in the recognition of the resistive load by mechanoreceptors or in the interpretation of the sensory input in patients with COPD.

This notion is consistent with the magnitude estimation studies of Gottfried et al in which the ability of COPD patients to consciously detect and quantify changes in airflow resistance was found to be impaired.

Zechman and Davenport pointed out that detection of flow-resistive loads occurs at midinspiration and corresponds to peak flow, while elastic loads are perceived towards the end of inspiration corresponding to maximal change in lung volume. He predicted that a resistive load should not interfere with the detection of elastic loads since at end inspiration air flow is zero. Our findings of a normal response to elastic loads in patients with chronic airways obstruction is consistent with their predictions.

The relationship between the respiratory sensations elicited by external loads and the magnitude of the neuromuscular response is still unclear. It seems reasonable to believe that the intensity of the sensation elicited by a load might influence the motor respiratory response.

REFERENCES


Q. (Cherniack): What happens to the FRC during CO2 rebreathing?
A. (Nochomovitz): We measured the FRC in 3 patients and there was no significant change from baseline.

Q. (Cherniack): What does an increased FRC do to the perception of external loading?

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<th>Pre-infusion</th>
<th>Post-infusion</th>
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<td>.38±.09</td>
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A. (Nochomovitz): I don't know.
C. (Altose): We have studied a group of patients who had recovered from acute respiratory failure. After recovery, one-half of them returned to normocapnia while approximately one-half remained hypercapnic. Although all patients had clear abnormalities of hypercapnic and hypoxic respiratory responses, abnormalities in respiratory sensation were noted only in those patients who remained in chronic respiratory failure.
Q. (Zwillich): Does abnormal load response predict which COPD patient will develop high Pco2?
A. (Nochomovitz): We don't know.

**Interaction Between Chemical Ventilatory Drive and Respiratory Compensation for Flow-Resistive Loading**


Normal individuals increase inspiratory effort during inspiratory flow-resistive loading. Several conditions have been shown to impair this response. These include anesthesia, brain hypoxia, sleep and chronic airways obstruction. Since all of these may be associated with blunting of chemical drive, and load compensation is tested during progressive hypercapnia, we determined whether alterations in ventilatory response to CO2 per se, could influence the respiratory compensation for flow-resistive loading. Ten goats were prepared with chronic tracheostomies and indwelling arterial and venous cannulae. Ventilatory and occlusion pressure (P100, as an index of inspiratory drive) responses to rebreathing CO2 in O2 were assessed before and after imposition of an inspiratory flow-resistive load of 25 cm H2O/L/sec. In five goats, studies were done before and during infusion of doxapram (3 mg/min); in the other five, studies were repeated 30 min after infusion of Tris buffer (15 mM/kg).

As anticipated, doxapram increased and Tris buffer decreased ventilatory responses to CO2. However, occlusion pressure responses to CO2 were enhanced by flow-resistive loading to an approximately equivalent degree before and after either drug. We thus conclude that the

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