Evidence of motor neuron involvement in chronic respiratory insufficiency

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SUMMARY Nineteen patients with chronic respiratory insufficiency, mean age 61.4 ± 12.2 , have been investigated with pulmonary function tests, clinical neurological examination and neurophysiological methods including motor and sensory conduction studies and needle electromyography. None of them had conditions known to affect the peripheral nervous system such as diabetes, alcoholism, or uraemia. The motor and sensory conduction studies showed only a reduced mean amplitude of the ulnar nerve SAP and of the compound muscle action potential of the APB and EDB muscles. The EMG was abnormal in 94.7% of the cases and showed an increased percentage of polyphasic potentials and a reduced recruitment pattern of motor units firing at high frequency. The data seem to support the hypothesis of an involvement of motor neurons in this condition although the evidence for a neuropathy is lacking.

While the effects of chronic respiratory insufficiency on the central nervous system are well known,¹⁻³ the influence of this condition on the peripheral nervous system has been the subject of clinical investigation only in recent years. Appenzeller *et al*⁴ reported the presence of a peripheral neuropathy in seven out of eight patients with chronic obstructive pulmonary disease. Clinical signs of peripheral nervous system involvement in 42 patients with chronic obstructive pulmonary disease were similarly observed by Wilner and Brody.⁵ More recently Faden *et al*⁶ compared the neurophysiological and clinical data of patients with chronic obstructive pulmonary disease with those obtained from age-matched controls with normal pulmonary function. Their findings seemed to indicate a subclinical sensory and motor neuropathy in the chronic obstructive pulmonary disease group.

The observation^{7,8} that some patients with chronic respiratory insufficiency do not show any satisfactory improvement during or after respiratory rehabilitative physical therapy might be related to the presence of a peripheral nervous system involvement. The aim of this study was to confirm

the presence of a peripheral nervous system involvement in a selected population of patients and eventually to identify the peripheral nervous system structure which was sensitive to the possible metabolic alterations induced by chronic respiratory insufficiency.

Material and methods

All the patients referred to the Cardiorespiratory and Physiotherapy Service of PA Trivulzio Hospital in 1982 were considered for the study. The respiratory physician excluded those suffering from conditions known to affect the peripheral nervous system, such as diabetes, alcoholism, uraemia, neoplasia, or neurotoxic drugs, and those who had undergone radiation treatment. Of the remaining 21 patients, two more were excluded: one in whom subclinical diabetes was present and one who, at the time of EMG, was suffering from an acute respiratory crisis. Finally 19 patients, 17 males and two females, mean age 61.4 years (± 12.2), affected by chronic respiratory insufficiency were studied.

The condition of chronic respiratory insufficiency was diagnosed according to the criteria established by the Societas Europae Phisiologia Clinicae Respiratoriae.⁹

Fifteen patients had obstructive ventilatory syndromes (five chronic bronchitis, nine chronic obstructive pulmonary disease, one pulmonary fibrosis) with Tiffenau index $<56\%$; two had restrictive syndromes (one bilateral pneumothorax, one chronic bronchitis + lobectomy) with Tiffenau index $>62\%$ and two had mixed ventilatory syndromes (one chronic bronchitis with pulmonary fibrosis

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Fig Evaluation of respiratory function in chronic respiratory insufficiency. Pulmonary function tests (RV, FEV₁, %FEV₁/VC) are expressed as %ΔNR versus NR. sGAW are expressed in SI units. Blood gases and Ac/Ba balance indexes are expressed in SI units (pO₂ and pCO₂), or as a percent (HbO₂), or in absolute units (pH). Chronic hypoxaemia and HbO₂ desaturation without respiratory acidosis is evident as the result of chronic obstructive lung disease.

Table 1 Degree of disability induced by chronic respiratory insufficiency (according to Rodman and Starling)

Class 1 (dyspnoea only during strenuous exertion)	6 patients
Class 2 (dyspnoea on climbing stairs)	9 patients
Class 3 (dyspnoea on walking)	4 patients
Class 4 (confined on chair or bed)	0 patients

and one chronic obstructive pulmonary disease) with Tiffenau index >62%.

Pulmonary function investigations

In each patient the following classical spirometric and mechanical indexes were determined: vital capacity (VC), forced expiratory volume at 1 second (FEV₁), residual volume (RV), specific conductance of airways (sGAW), resistance of airways (RAW). The evaluation of the pulmonary diffusion was carried out with the single breath method (TLCO) and blood gas determinations completed the study; none of our patients had respiratory alkalosis (fig).

Clinical examination

A complete physical and neurological examination was performed in all patients. The clinical evaluations of respiratory function followed the criteria established by Rodman and Straling¹⁰ (table 1). The history was also

taken and the smoking habits of the patients were considered (cigarettes/day/years of consumption).

Electrodiagnostic tests

Motor and sensory conduction studies were performed in each patient using surface electrodes. The temperature was controlled and kept between 34°C – 35°C in the upper limbs and 32°C ± 33°C in the lower limbs. The sensory action potentials (SAPs) of the median and ulnar nerves were determined stimulating orthodromically the digital fibres and recording at the wrist. The sural nerve SAP was obtained stimulating the nerve antidromically just lateral to the midline in the posterior portion of the calf at 7–14–21 cm from the recording electrode placed just below and behind the lateral malleolus. The motor conduction velocity (MCV) was measured in the median and peroneal nerves. The median nerve was stimulated at the wrist and elbow and the compound muscle action potential (CMAP) was recorded from the abductor pollicis brevis. The peroneal nerve was stimulated at the ankle and just below the fibular head and the recording electrodes were placed on the extensor digitorum brevis. The EMG examination was carried out in the biceps brachii and tibialis anterior muscles and a quantitative analysis of the EMG was performed in both muscles. The amplitude, duration and number of phases were calculated in 20 motor unit action potentials (MUAPs), each of them recorded at least three times. The onset and termination of the potentials were defined by a deflection from baseline of more than 20 μV.

Table 2 Conduction studies

	Median SAP				Ulnar SAP				Sural SAP			
	Amplitude		Latency		Amplitude		Latency		Amplitude		Latency	
	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM
All patients (n = 19)	15.4	2.5	2.8	0.04	8.9*	1.3	2.6	0.06	11.0	1.0	3.6	0.07
Patients <65 yr (n = 10)	22.1	3.0	2.7	0.04	13.3	1.3	2.5	0.05	12.5	1.4	3.6	0.09
Controls (n = 18)	21.4	2.1	2.6	0.04	13.5*	1.1	2.4	0.04	13.2	0.9	3.5	0.07
	NS		NS		p < 0.02*		NS		NS		NS	
	Median motor				Peroneal motor							
	CV		DL		Amplitude		CV		DL		Amplitude	
	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM
All patients (n = 19)	60.5	1.0	3.5	0.1	7.1*	0.5	47.8	0.9	4.1	0.1	3.9*	0.4
Patients <65 yr (n = 10)	60.5	1.2	3.5	0.1	7.4	0.7	49.2	1.1	3.9	0.1	4.0	0.4
Controls (n = 18)	61.2	0.9	3.3	0.1	10.5*	1.1	48.7	0.9	3.8	0.1	7.2*	0.7
	NS		NS		p < 0.001*		NS		NS		p < 0.001*	

Amplitude is expressed in μV (SAPs) or mV (MCV).

Duration is in milliseconds.

CV = conduction velocity.

p values are calculated between the means marked by *.

The neurophysiological data were compared with those obtained from a control groups of 18 healthy subjects, mean age 59.7 years (± 13.2).

Results

Neurological examination showed abnormalities in nine patients but in six of them the only finding was a mild vibratory sensory loss of doubtful clinical importance. Of the remaining three patients, two had reduced deep tendon reflexes in the lower limbs and one showed some distal muscle wasting and fasciculations in the thighs.

The mean and SEM of the nerve conduction and EMG findings are summarised in tables 2 and 3. MCVs were normal in all patients but the mean amplitude of the CMAPs recorded from the abductor pollicis brevis and extensor digitorum brevis muscles were significantly different from the control values (table 2). However no significant decrement of the CMAP amplitudes recorded after proximal stimulation of the nerves was evident and the morphology of the CMAPs did not reveal slowing of conduction

of the nerve fibres. The sensory conduction studies were always normal in the sural nerve while six patients (31%, all aged over 65 years) showed some alteration in the median and ulnar nerve SAPs. The latter was absent in two patients and of reduced amplitude and slightly prolonged latency in four; the median SAP could not be recorded in one case and its amplitude was reduced in two.

In the concentric needle EMG seven patients (36.6%, five aged over 65 years) showed fibrillation potentials in at least three areas of each of the muscles tested. In 12 patients (63.1%, six aged over 65 years) the MUAPs recruitment showed a transitional or reduced interference pattern. The percent of polyphasic potentials was increased in one or two muscles of 15 subjects (78.9%, eight aged over 65 years), the upper limit being 12% and 20% in the biceps and tibialis anterior respectively (table 3).^{11 12}

While the mean ulnar nerve SAP amplitude fell within the normal range after the exclusion of the patients aged over 65 years, the other parameters, that is the mean amplitude of the CMAPs, the per-

Table 3 EMG data

	Biceps brachii				Tibialis anterior			
	Duration		% Polyph		Duration		% Polyph	
	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM	$\bar{X}$	SEM
All patients (n = 19)	10.7	0.4	20.2*	2.0	12.0	0.4	17.9*	2.0
Patients <65 y (n = 10)	10.9	0.6	19.6	3.3	11.7	0.5	21.0	2.4
Controls (n = 18)	10.5	0.4	4.8*	1.1	12.1	0.4	8.7*	1.4
	NS		p < 0.001*		NS		p < 0.001*	

Duration in milliseconds. p values are calculated between the means marked by *.

cent of polyphasic potentials and the pattern of recruitment did not change.

Pulmonary function expressed by spirometric values (FEV₁), arterial blood gases levels (pO₂, pCO₂) and the percent of HbO₂ did not correlate significantly with the abnormal electrophysiological parameters quantitatively evaluated (CMAP amplitude of the abductor pollicis brevis and extensor digitorum brevis muscles and the percent of polyphasic potentials). The smoking habits of the patients also were not significantly correlated with the above-mentioned parameters. However, a slightly positive Spearman's correlation coefficient was present when the percent of HbO₂ was correlated with the amplitude of the CMAP of the abductor pollicis brevis and extensor digitorum brevis muscles (0.62 and 0.59 respectively).

Discussion

The nerve conduction studies carried out in our patients did not reveal any slowing of sensory and motor conduction but showed a reduced mean amplitude of the ulnar nerve SAP and of the CMAP of abductor pollicis brevis and extensor digitorum brevis muscles (table 2). The first finding is probably related to a subclinical compressive neuropathy at the elbow, quite common in the elderly;¹³ this hypothesis is supported by the normal value of the ulnar nerve SAP mean amplitude obtained after the exclusion of the patients over 65 years. The reduced mean amplitude of the CMAPs which is mainly an expression of the number and size of the active motor units¹⁴ and the lack of conduction block or slowing in the distal segments of the motor nerve indicates that the decreased number of active motor units is probably a consequence of a reduced number of motor neurons and not of a damage of the peripheral nerve. The EMG studies were abnormal in 94.7% of the cases (table 3), showing a striking increase of polyphasic potentials and a reduced recruitment pattern of MUAPs firing at high frequency. These findings, in the face of normal conduction studies, suggest an involvement of the motor neurons. It is worth underlining the slightly positive correlation coefficient of the percentage of HbO₂ plotted against the amplitude of the CMAPs, even if it is not statistically significant. The percentage of HbO₂ reflects the O₂ available for the metabolism of the neurons, whose number is reduced in our case as shown by the CMAPs' amplitude and by the reduced recruitment pattern. The pO₂,⁶ on the other hand, might be only an expression of the ventilatory compensation mechanisms.

Appenzeller *et al*⁴ found a marked slowing of the MCV in the peroneal nerve of patients with chronic

obstructive pulmonary disease. These findings can be explained if their subjects were selected on the basis of weight loss and malnourishment. There was a great variability of the clinical features of the neuropathy and in some patients the nerve conduction improved after correction of the diet. Therefore, a possible role of other pathogenetic factors related to nutritional deficiencies cannot be excluded.

Other authors^{5, 15} have reported a significant incidence of clinical signs of sensori-motor neuropathy in patients with chronic obstructive pulmonary disease, but in these studies no attempt was made to exclude other possible causes of nerve involvement and neurophysiological studies were not performed.

An association of chronic respiratory insufficiency and subclinical neuropathy was found by Faden *et al*.⁶ They reported the presence of slowing of motor and sensory conduction in 87% of their cases. Since no information was given on the degree of disability of the patients, we cannot exclude the presence of a compressive neuropathy in subjects who are bed-ridden or confined to a wheel-chair. In their study, only smoking habits were correlated to the impairment of sensory nerve function, while no correlation was found between nerve conduction and the pulmonary function. When comparing our results, there was a striking difference in the percent of EMG abnormalities represented by the presence of polyphasic MUAPs and of a reduced recruitment pattern. They found some EMG alterations in only 20% of the cases, all with impaired conduction studies, while we were able to demonstrate some EMG abnormalities in 94.7% of the patients. This difference might be due to the adoption of quantitative methods that allow an objective evaluation of the EMG and the unbiased detection of prolonged and/or polyphasic potentials.

To summarise, our data suggest the presence of motor neuron damage in our subjects, in disagreement with other reports that indicate an involvement of the peripheral nerves in patients with chronic respiratory insufficiency. These conclusion are in line with various studies that demonstrate the greater susceptibility of the spinal cells to anoxia and the relative resistance of the peripheral nerve.^{16, 17}

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