Phrenic nerve conduction time in Guillain-Barré syndrome

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SUMMARY Phrenic nerve conduction was studied in 28 patients with Guillain-Barré syndrome. Conduction time was prolonged in 18 (64.3%) patients and serial studies showed progressive improvement with restoration of normal values in the majority by 12 weeks. The conduction abnormalities had a positive correlation with the extent of the disease, morbidity and mortality. Phrenic nerve conduction time was found to be a more sensitive parameter than vital capacity or median nerve motor conduction velocity in assessing the severity of the disease and predicting impending ventilatory failure.

A simple technique of determining phrenic nerve conduction in man *in vivo* has been described by Newsom Davies.¹ He demonstrated that the diaphragmatic muscle action potential can be recorded by surface electrodes placed over the lower intercostal spaces and confirmed that it represented the true diaphragmatic muscle action potential, firstly, by the observation that this response preceded the mechanical response of the chest wall to diaphragmatic twitch, and secondly, by finding that the response obtained by direct recording from indwelling diaphragmatic electrodes and by surface electrodes occurred almost synchronously. In local lesions of the phrenic nerve and in peripheral neuropathy due to a variety of causes, the phrenic nerve conduction time was found to be prolonged.

In clinical practice, it is important to know the severity and extent of involvement of disease in Guillain-Barré syndrome. Determination of motor conduction of limb nerves does not necessarily reflect the severity of the disease process and may even be normal in the presence of severe motor weakness.^{2,3} Detection of early signs of ventilatory failure is of paramount importance in the management of Guillain-Barré syndrome. Fluoroscopic examination of the diaphragm has been found to be of limited value when both halves are paralysed⁴ and

alteration in vital capacity was not of value in predicting ventilatory failure, particularly in early stage of the illness.¹

The present work was designed, (a) to find out the frequency of involvement of phrenic nerve in Guillain-Barré syndrome, (b) to evaluate the value of phrenic nerve conduction time in predicting ventilatory failure and (c) to correlate the changes with severity and outcome of the disease.

Material and methods

Thirty two healthy volunteers with no evidence of peripheral neuropathy or pulmonary disease formed the control group. During the period of study of one year, 28 patients with Guillain-Barré syndrome were examined. The diagnosis was based on the criteria suggested by Masucci and Kurtzke.⁵ Phrenic nerve conduction was performed within 24 hours after admission and further serial recordings were done at intervals to assess progress. Clinical features of overt ventilatory failure such as breathing difficulty, impaired chest expansion, vital capacity and motor conduction velocity of the median nerve were recorded.

Procedure

Phrenic nerve conduction was studied according to the procedure described by Newsom Davis.¹ The patient lay supine with head slightly elevated and rotated to the side opposite to the nerve under stimulation. The stimulus was a rectangular pulse of 0.2 to 1.0 ms duration, delivered at a frequency of 1 Hz. The phrenic nerve was stimulated percutaneously in the neck at the posterior border of the sternomastoid at the level of the upper margin of the thyroid cartilage. The cathode was a circular saline pad 1 cm in diameter and the anode was a metal plate applied over the

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Received 1 May 1984 and in revised form 12 August 1984.
Accepted 23 August 1984

manubrium sterni. Surface recording electrodes were placed 3.5 cm apart in the eighth or the ninth intercostal space with anterior electrodes in the anterior axillary line. The ground electrode consisted of a metal plate strapped over the chest wall. By careful placement of the electrode, it was possible to localise accurately the stimulation to the phrenic nerve and avoid brachial plexus stimulation. The pulse rate and blood pressure were monitored during the procedure of stimulation. The latency of the diaphragmatic muscle action potential was measured from the stimulus artefact to the onset of the potential. The duration and the peak to peak amplitude of the muscle action potential were also determined. The height of the individual was recorded.

Percutaneous stimulation of the median nerve was done at the wrist and the elbow with supramaximal current and the muscle action potential was recorded from the abductor pollicis brevis with needle electrodes. Vital capacity predicted for the height, age and sex was determined. Less than 80% of the predicted value was considered indicative of ventilatory insufficiency.

Fig 1 Diaphragmatic muscle action potential in a control subject.

Fig 2 Values of phrenic nerve conduction time, duration and amplitude of diaphragmatic muscle action potential in 32 control subjects.

Results

Controls

Figure 1 shows the diaphragmatic muscle action potential in a control subject. The values for phrenic nerve conduction in 32 healthy individuals of age ranging from 14 to 62 years are shown in fig 2. There were 20 males and 12 females. The mean conduction time was 7.4 ± 0.9 (SD) ms, and the mean duration of diaphragmatic muscle action potential was 28.2 ± 4.4 (SD) ms. The amplitude varied over a wide range, hence was not considered to be of diagnostic value (mean 509 ± 122.2 (SD) μV). There was no correlation of conduction time with age or sex, but phrenic nerve conduction time showed significant positive correlation with height ($r = 0.86$, $p < 0.001$). Figure 3 depicts the phrenic nerve conduction time as a function of height. The regression line of height on conduction time was $Y = 0.0653X - 3.0613$, and the regression coefficient was 0.0653 which was significant ($p < 0.001$). Alteration in pulse rate or blood pressure was not seen during stimulation of the phrenic nerve.

Patients

The age of the patients varied from 12 to 60 years; there were 23 males and five females. All the 28 patients had weakness of both lower limbs, 23 of them also had weakness of upper limbs and in 15 subjects all four limbs and trunk muscles were affected (table 1). Cranial nerves were involved in eight patients. All of them had varying degree of motor weakness of limbs. In all these patients, IX and X nerves were affected, and in four of them

Fig 3 Phrenic nerve conduction time as a function of height in 32 control subjects. The regression line of height on conduction time is shown.

Phrenic nerve conduction time in Guillain-Barré syndrome

Table 1 Clinical features and phrenic nerve conduction time in 28 patients of Guillain-Barré syndrome

Neurological deficit	Number of patients	Phrenic nerve conduction time Normal	Abnormal
Lower limbs	5	4	1
All 4 limbs	8	3	5
All 4 limbs + trunk muscles	7	2	5
Cranial NS + 4 limbs + trunk muscles	8	1	7

there was evidence of bilateral VII nerve involvement and in one patient of the latter group, oculomotor nerves were also affected. In nine patients mild sensory impairment, confined to distal parts of limbs, was present. Twenty three patients with weakness of all four limbs had sluggish to absent tendon reflexes in all the limbs. In the five patients with weakness confined to lower limbs, tendon reflexes were absent in the lower limbs in all, sluggish in upper limbs in two and normal in three patients.

Abnormalities in phrenic nerve conduction time were observed in 18 of the 28 patients (64.3%) at admission or on subsequent examination. The conduction time values shown in table 2 are the values correlated for the height of the individual. In two of them (Case 3 and 28) the nerve was found to be inexcitable. In one patient (Case 18) the first recording done on 14th day was normal, but on the 30th day phrenic nerve conduction time was prolonged with subsequent decline to normal values. In the rest 10 patients, the phrenic nerve conduction time was normal on serial recordings. Since the duration of muscle action potential did not differ significantly in patients as compared to controls, this parameter was not considered useful in diagnosis.

Fig 4A, 4B Serial values of phrenic nerve conduction time in 18 patients of Guillain-Barré syndrome who had abnormal conduction. Individual cases are shown and are indicated by case number. NR—no response; PNCT—phrenic nerve conduction time.

Table 2 Phrenic nerve conduction time in 28 patients with Guillain-Barré syndrome

No	Day	Phrenic nerve conduction time ms	Median Mcv m/s	Vital capacity (% predicted)	No	Day	Phrenic nerve conduction time ms	Median Mcv m/s	Vital capacity (% predicted)
1	28	10.7*	41.6*	75.8*	15	15	12.6*	41.6*	90.0
2	14	7.7	60.0	85.4	16	14	15.4*	26.5*	48.8*
3	6	NR*	27.0*	46.2*	17	18	15.8*	34.0*	56.9*
4	14	15.4*	38.8*	63.2*	18	14	7.7	49.0	92.0
						30	10.8*	58.0	90.6
5	12	6.5	57.0	84.2	19	8	6.2	60.0	90.4
6	11	6.2	50.0	95.3	20	16	18.0*	19.8*	51.8*
7	8	6.9	66.0	88.9	21	8	6.1	52.4	93.3
8	3	10.8*	34.0*	48.0*	22	6	7.6	62.0	90.2
9	11	12.8*	39.0*	86.4	23	14	12.3*	33.8*	68.8*
10	15	16.2*	26.0*	56.6*	24	12	9.3*	64.6	88.4
11	3	10.8*	60.0	90.0	25	7	6.2	59.8	92.6
12	14	12.3*	43.0*	58.4*	26	23	9.6*	55.4	90.8
13	6	6.9	62.8	88.6	27	8	9.8*	57.6	84.0
14	8	6.2	57.0	93.2	28	5	NR*	35.8*	63.5*

(* indicates abnormal value)

Table 3 Phrenic nerve conduction time and morbidity and mortality in 28 patients with Guillain-Barré syndrome

Phrenic nerve conduction time	Fatal	Residual disability	Complete recovery
Normal (10)	0	2 (20%)	8 (80%)
Prolonged (18)	2 (11.1%)	11 (61.1%)	5 (27.8%)

On serial recordings it was seen that in the 18 patients with prolonged phrenic nerve conduction time, there was progressive improvement of phrenic nerve conduction, with decrease in the conduction time (fig 4). In five patients by 8 weeks, in nine patients by 12 weeks, in three patients by 16 weeks and one patient by 20 weeks, normal values for conduction time were observed. Thus by the end of 12 weeks, in 14 of 18 (77.8%) and by the end of 16 weeks in 17 of 18 (94.4%) patients, full recovery of phrenic nerve conduction was observed.

The relative diagnostic value of clinical evidence of respiratory failure, vital capacity, median nerve conduction and phrenic nerve conduction time was evaluated. Clinical evidence of ventilatory failure was seen in six patients, reduced vital capacity in 11, slowing of median motor conduction velocity in 13 and prolonged phrenic nerve conduction time in 18 patients. It is seen that in 10 patients with normal phrenic nerve conduction time, all other parameters were also within the normal range. None of these patients required intensive care in respiratory unit during the course of illness. At the time of examination, of the 18 cases with abnormal phrenic nerve conduction time, in 12 there was no clinical evidence of ventilatory disturbance, in seven the vital capacity was normal and in five the median nerve conduction velocity was normal. When the latter three parameters were considered together, there was no further improvement of diagnostic yield. Of these 18 patients with prolonged phrenic nerve conduction time, 15 (83.3%) required respiratory assistance at some stage during the period of observation in the hospital and three patients did not develop ventilatory failure.

An attempt was made to relate the abnormalities of phrenic nerve conduction to the extent of the disease and the final outcome. It is clear from table 1, that phrenic nerve conduction abnormalities were more frequently present in cases with widespread involvement. It was also seen that the residual disability was less frequent and full recovery was more common in patients with normal phrenic nerve conduction (table 3).

Discussion

Mortality in Guillain-Barré syndrome due to ventilatory failure is around 20%.⁶ Early recognition and timely institution of appropriate measures result

in considerable reduction of mortality.⁷ Clinical assessment and vital capacity measurement though useful, are not sensitive enough to detect ventilatory failure in the early stages.¹ From the present findings and the report of Newsom Davies¹ it is seen that phrenic nerve conduction studies provided the earliest indication of involvement of respiratory muscles and in most instances heralded ventilatory insufficiency. In clinical practice this warning was used to advantage in selection of patients who might require respiratory assistance in future. In the present series 83.3% of patients with prolonged phrenic nerve conduction time, developed ventilatory failure during the course of the illness.

Earlier attempts to record the diaphragmatic muscle action potential involved the use of oesophageal electrodes⁸ or needle electrodes inserted through the chest wall.⁹ For obvious reasons these procedures are both cumbersome and unpleasant to the patient. The technique described by Newsom Davies¹ of recording the muscle action potential by surface electrodes placed over the chest wall has eliminated the problems encountered with the previous procedures. Bradycardia or alteration of blood pressure were not observed during the procedure of phrenic nerve stimulation. Charniak *et al*¹⁰ noted oscillations in blood pressure associated with phrenic nerve stimulation. In the present study the absence of such effects may be because the stimuli were delivered only for a short duration.

In the present series phrenic nerve conduction was found to be abnormal in 64.3% (18 of 28 patients) while decrease in median motor conduction velocity was seen only in 46.4% (13 of 28 cases). In no single case was abnormal median nerve conduction velocity with normal phrenic nerve conduction noted, indicating the sensitivity and the diagnostic importance of phrenic nerve conduction. Newsom Davies,¹ however observed that forearm conduction velocity was directly related to phrenic nerve conduction time.

Phrenic nerve conduction abnormality was found to be of value in predicting the severity of the disease and prognostication in terms of morbidity and mortality. The disease process was more severe and final outcome poorer in the patients with delayed conduction compared to those with normal conduction.

It is of interest that the conduction abnormality persisted up to a maximum of five months after the

onset of illness and full clinical recovery had preceded the electrophysiological recovery. These findings are in agreement with the observations of other workers who noted persistence of decrease in conduction velocity of peripheral limb nerves in Guillain-Barré syndrome even after full clinical recovery.¹¹

The simplicity of the technique and the information yield are adequate justifications for routine determination of phrenic nerve conduction in generalised neuropathies, particularly acute infectious polyradiculoneuritis, with an inherent risk of developing ventilatory insufficiency, for predicting impending respiratory failure.

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