SHORT REPORT

Respiratory electrophysiological studies in Guillain-Barré syndrome

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Abstract

Respiratory failure is a common and potentially life threatening complication in patients with Guillain-Barré syndrome. The incidence of phrenic nerve involvement and the predictive value of phrenic nerve conduction and diaphragmatic needle EMG were studied in 40 patients with Guillain-Barré syndrome within the first three days of admission to hospital. The negative peak onset latency of the diaphragmatic compound muscle action potential (CMAP), and its amplitude, duration, and area were abnormal in 83%. The need for ventilation was correlated with diaphragmatic CMAP amplitude (P = 0·005), and area (P = 0·001), but not with latency or duration. Abnormalities in diaphragmatic needle EMG were found in 45%, mainly a decreased number of motor unit potentials. The abnormalities correlated with the need for ventilation (P = 0·013). Of the 40% who required ventilation, all had either abnormal phrenic conduction, abnormal diaphragmatic needle EMG, or both. Eighty one per cent of the ventilated patients had abnormal forced vital capacity on the day of the electrophysiological examination.

The results indicate that phrenic nerve conduction studies and diaphragmatic EMG are useful in detecting respiratory involvement in patients with Guillain-Barré syndrome and in identifying those at risk of respiratory failure.

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Respiratory failure requiring mechanical ventilation is a common complication of Guillain-Barré syndrome and occurs in 14–44% of patients.[1 2] Ventilatory failure in Guillain-Barré syndrome is primarily due to diaphragmatic weakness, although weakness of intercostal, abdominal, and accessory muscles of respiration, retained airway secretions, atelectasis, and supine posture are also contributory factors.[3] Early recognition of those at risk of respiratory decompensation is important as they may benefit from intensive monitoring and early treatment. Arterial blood gas analysis, forced vital capacity (FVC), and clinical assessment are relatively insensitive methods of detecting ventilatory failure in the early stages of Guillain-Barré syndrome.[4]

Gourie-Devi and Ganapathy reported that the phrenic nerve latency is useful in predicting disease severity, morbidity, and mortality in patients with Guillain-Barré syndrome,[5] but other electrophysiological features of the respiratory system have not been studied. We have further developed the technique of phrenic nerve conduction study and needle EMG of the diaphragm, and found them valuable in the investigation of neuromuscular respiratory failure.[6] Hence, the aim of the present work is to describe the range of electrophysiological abnormalities of the respiratory system in patients with Guillain-Barré syndrome, and to determine the predictive value of these relevant electrophysiological studies. Preliminary reports have been given.[7 8]

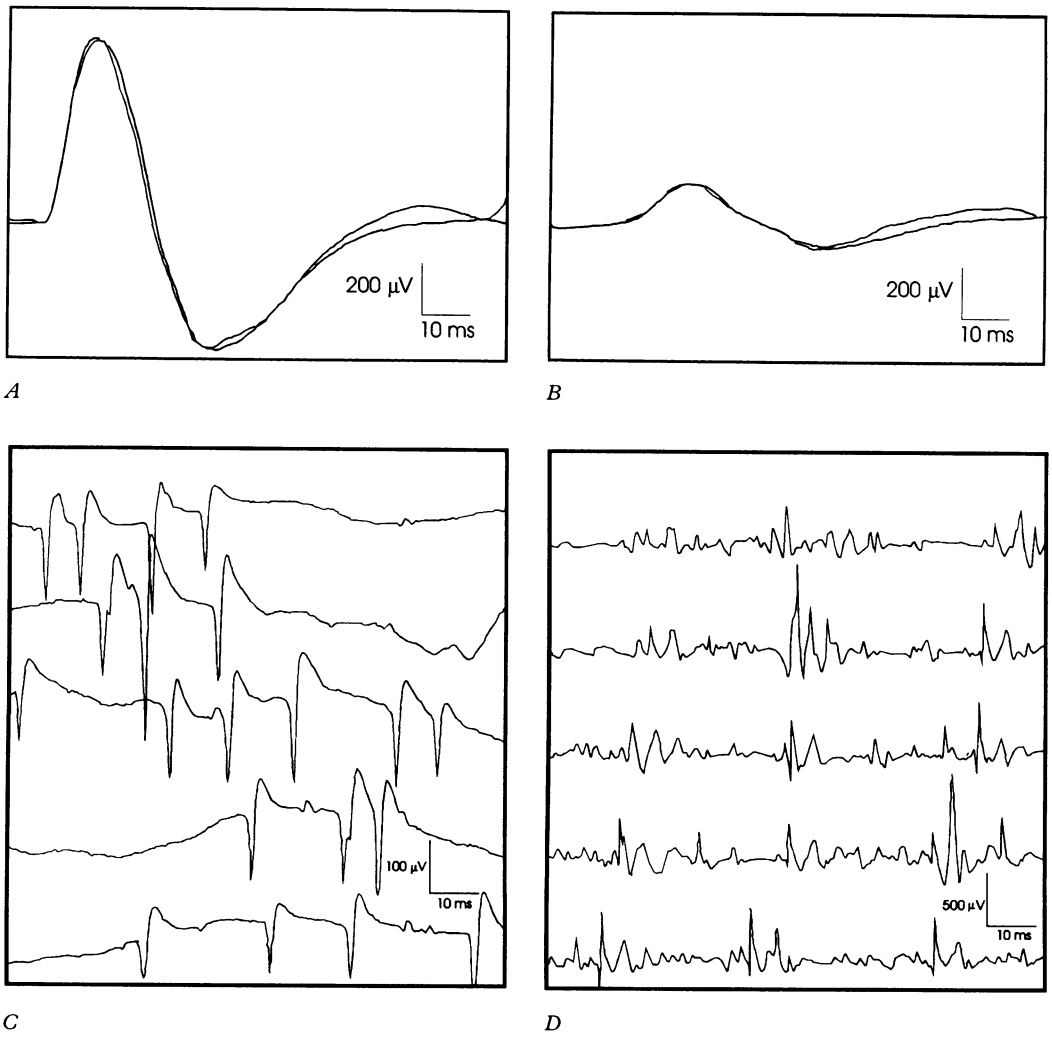
Material and methods

PATIENT SELECTION

The hospital and EMG charts of all patients with Guillain-Barré syndrome admitted to Victoria Hospital, London, Ontario between January 1991 and January 1995 were reviewed according to a detailed protocol. There were 47 patients who had had phrenic nerve conduction measurements and needle EMG of the diaphragm. Seven patients were excluded because of other neurological diseases as well as Guillain-Barré syndrome, and pre-existing metabolic and cardiopulmonary disorders. Thus 40 patients were reviewed (24 men and 16 women, mean (range) age 51 (18–82) years). One patient had an axonal type of Guillain-Barré syndrome.[9] All other patients had a primary demyelinating type.

ELECTROPHYSIOLOGICAL STUDIES

Electrophysiological examinations were performed within 1·2 (range 0–3) days of admission, 8·3 (range 2–28) days after the onset of symptoms. Nerve conduction studies and needle EMG were performed with an Advantage EMG machine (Clark Davis Medical Systems,



(A) Right phrenic nerve conduction study in an 80 year old, healthy man. Onset of latency 7·8 ms; diaphragmatic CMAP amplitude 710 μV; area of the CMAP: 9·0 mVms; duration of the CMAP 21·4 ms. (B–D) Phrenic nerve conduction study and diaphragmatic needle EMG on the 18th day after onset of Guillain-Barré syndrome in a 42 year old man. At the time of EMG, FVC was 3·2 l (64% of the predicted value). The patient had to be ventilated three days later. The studies were consistent with moderate demyelination of the phrenic nerve and some axonal degeneration with resulting denervation of muscle. (B) Abnormal right phrenic nerve conduction study; onset of latency 16·3 ms; diaphragmatic CMAP amplitude 155 μV; area of CMAP 2·1 mVms; duration of CMAP 25·8 ms. (C) Right diaphragmatic needle EMG during quiet breathing; positive sharp waves were recorded between inspiratory bursts of motor unit potentials. (D) Right diaphragmatic needle EMG during quiet breathing. During inspiration the number of motor unit potentials recorded was reduced, but was not clearly abnormal in morphology.

London, Ontario, Canada) according to standard techniques.[10] Phrenic nerve conduction studies were performed with percutaneous stimulation in the supraclavicular fossa, and recording from the ipsilateral diaphragm with surface electrodes.[11] Four measurements of the diaphragmatic CMAP were determined: the latency to the onset of the negative peak; the CMAP amplitude from the baseline to the negative peak; the negative peak area; and the CMAP duration from the negative peak onset to the return to baseline (figure, A). Needle EMG of the diaphragm was performed with a monopolar needle electrode inserted between the anterior axillary and medial clavicular lines, just above the costal margin.[12]

SPIROMETRY AND MECHANICAL VENTILATION

The FVC was obtained on the day of electrophysiological studies and during the subsequent four weeks with a spirometer (Pocket spirometer, Micro Medical Instrument, Kent, UK). Predicted values were calculated from sex, age, and height with a standard formula.[13] Values of FVC were considered abnormal if they were below 80% of the predicted value.

STATISTICAL ANALYSIS.

The relation between results of nerve conduction studies and FVC were analysed by simple regression analysis. The relation between diaphragmatic needle EMG (normal/abnormal) and the need for mechanical ventilation was evaluated by χ^2 test. The results of nerve conduction studies in the ventilated group and the non-ventilated group were compared by unpaired t test (two tailed). Differences were considered statistically significant if $P \leqslant 0{\cdot}05$.

Results

PHRENIC AND MEDIAN NERVE CONDUCTION STUDIES

Phrenic nerve conduction was abnormal in 33 (83%) patients (table; figure, B). The features of the diaphragmatic CMAPs were: latency 9·1 (SD 1·5) ms, delayed in 31 (78%); amplitude 408 (SD 207) μV, reduced or absent in 17 (43%); negative peak area 4·7 (SD 2·5) μVms, reduced or absent in 23 (58%); duration 21·6 (SD 4·2) ms, prolonged in 13 (33%). The diaphragmatic CMAP was not recordable on either side in one patient. The only patient with the pure axonal type of Guillain-Barré syndrome had normal phrenic nerve conduction.

Median nerve motor conduction studies were abnormal in 32 (80%) patients: distal motor latency 6·8 (SD 3·8) ms, prolonged (> 4·7 ms) in 26 (65%); thenar CMAP 4·8 (SD 3·3) mV, diminished (< 4·0 mV) in 19 (48%); forearm conduction velocity 47·0 (SD 7·8) ms, reduced in 17 (43%).

Phrenic nerve conduction: normal values (n = 25) and results in patients with Guillain-Barré syndrome*

Measurement	*Normal subjects (mean (SD))*	*Normal limit*	*Guillain-Barré syndrome ventilated (n = 16)* (mean (SD))*	*Guillain-Barré syndrome not ventilated (n = 24)* (mean (SD))*
Latency (ms)	6·5 (0·8)	< 8·1†	9·0 (1·4)	9·1 (2·0)
Amplitude (μV)	660 (201)	> 300‡	324 (167)	464 (239)
Negative peak area (μVms)	7·3 (2·1)	> 4·0‡	3·5 (1·8)	5·4 (2·6)
Negative peak duration (ms)	19·4 (2·7)	< 25†	21·5 (4·3)	21·6 (4·5)

*Both phrenic nerves were studied in each subject or patient.
†Upper limit of normal calculated as mean + 2 SD.
‡Lower limit of normal based on distribution of normative data.

DIAPHRAGMATIC EMG

Abnormal diaphragmatic EMGs were found in 18 (45%). Three (8%) had denervation potentials, fibrillation potentials, and positive sharp waves (figure, C). Fifteen (38%) had a decreased number of motor unit potentials firing (figure, D). Two of these 15 patients had normal phrenic nerve conduction studies; both patients had to be ventilated during the course of the disease. In four patients the motor unit potentials were polyphasic. The diaphragmatic EMG was normal in the patient with axonal Guillain-Barré syndrome.

SPIROMETRY AND MECHANICAL VENTILATION

The mean FVC on the day of the EMG was 2·6 (SD 1·6) l. In 16 (40%) patients the FVC was below 80% of the predicted value. Five patients with normal FVC on the day of EMG had abnormal FVC during the subsequent four weeks; three of them had to be ventilated during the course of disease.

Mechanical ventilation was required in 16 (40%). Ventilation was started nine (range 3–28) days after the onset of symptoms. The mean duration of ventilation was 31 (range 4–59) days.

CORRELATION BETWEEN ELECTROPHYSIOLOGY AND RESPIRATORY FAILURE

Patients who required mechanical ventilation had significantly lower diaphragmatic CMAP amplitude (P = 0·005), smaller negative peak area (P = 0·001), and lower thenar CMAP (P = 0·011) than those who did not require ventilation. No relation was found between phrenic nerve latency, duration of the diaphragmatic CMAP, distal median motor nerve latency, median motor nerve conduction velocity, and the need for ventilation. Abnormal diaphragmatic EMG findings correlated with the need for mechanical ventilation (P = 0·013).

There was a significant correlation among the FVC and the diaphragmatic CMAP amplitude (P = 0·0003, r = 0·546), the negative peak area (P = 0·0004, r = 0·538), and abnormal diaphragmatic needle EMG (P = 0·0024). The median nerve conduction velocity (P = 0·0005, r = 0·526) and thenar CMAP (P = 0·0021, r = 0·472) also correlated significantly with the FVC. Despite these correlations the FVC at the day of EMG was abnormal in only 13 of 16 ventilated patients. There were no significant correlations among the phrenic nerve latency, the duration of the diaphragmatic CMAP, or the median nerve latency, and the FVC.

All 16 patients who required mechanical ventilation showed either abnormal phrenic nerve conduction (14, 88%), abnormal diaphragmatic EMG (11, 69%), or both abnormalities (9, 56%). Three of the 16 ventilated patients had normal median nerve conduction studies. Among the 24 patients who did not require ventilation, 19 (79%) had abnormal phrenic nerve conduction studies and seven (29%) also had abnormal diaphragmatic EMG. The five patients with normal respiratory electrophysiological studies did not require ventilation. Forty two per cent of patients with abnormal phrenic nerve latency, 82% with diminished diaphragmatic CMAP amplitude, and 78% with abnormal diaphragm EMG required mechanical ventilation.

Discussion

Our findings indicate that involvement of the phrenic nerve and diaphragm is common at an early stage of the disease, occurring in 88% of patients. Furthermore, some respiratory electrophysiological variables are sensitive predictors of severe respiratory failure, and are superior to spirometry in terms of early recognition of patients who are at risk of severe diaphragmatic weakness.

A prolonged phrenic nerve latency was the most common finding (78%), being present in ventilated as well as in non-ventilated patients. This suggests that either axonal degeneration or mild segmental demyelination is occurring in the early stages of Guillain-Barré syndrome; the prolongation was only mild and did not correlate with the FVC or with the need for ventilation. However, features other than the prolonged latency proved important. The diaphragmatic CMAP amplitude and negative peak area were both reduced, but the duration was unchanged. This suggests that either axonal degeneration or demyelination caused a pure conduction block in phrenic nerve fibres distal to the point of stimulation in the neck. Prolongation of the duration of the diaphragmatic CMAP would have indicated disproportionate slowing of conduction in nerve fibres that were not blocked. This, plus the only mildly prolonged latency, suggest that phase cancellation was unlikely to have been an important mechanism of CMAP amplitude and area reduction. In the early course of Guillain-Barré syndrome, conduction block in primarily demyelinated but otherwise intact motor nerve fibres cannot be

distinguished from "axonal conduction block" in nerve fibres undergoing active degeneration, in which portions of the axons remain excitable and capable of impulse transmission for up to five days.[14] Only serial phrenic nerve conduction studies and needle EMG of the diaphragm would distinguish these two mechanisms.[15 16] However, because our studies were performed 8·3 (2–28) days after onset of symptoms, we believe demyelinating conduction block was present in most patients.

The diaphragmatic EMG was complementary to phrenic nerve conduction in detecting involvement of the phrenic nerve in Guillain-Barré syndrome. A moderate to severe decrease in the number of units was the most common abnormality, which we attributed either to conduction block or early axonal degeneration of the phrenic nerve. In two patients there was a severely decreased recruitment of motor unit potentials in the presence of normal phrenic nerve conduction, likely due to conduction block proximal to the point of phrenic nerve stimulation in the neck; both patients later required mechanical ventilation. Fibrillation potentials and positive sharp waves are known to appear in muscles as a sign of denervation 10–20 days after axonal damage. In our patients the EMG was performed eight (range 2–28) days after onset of symptoms, and only three patients had denervation potentials in the diaphragm. Thus it may have been too early in some patients for this sign of denervation to have appeared. Needle examination of the diaphragm was well tolerated in all patients. No complications, such as pneumothorax, were found.

Although phrenic nerve conduction and needle EMG of the diaphragm showed a sensitivity of 100% in predicting respiratory failure, they were not specific. Patients without respiratory failure had abnormal phrenic nerve latencies (79%), abnormal diaphragmatic CMAP amplitudes (29%), and abnormal findings on needle EMG of the diaphagm (29%). However, no patient with normal electrophysiological respiratory studies developed respiratory failure. Thus patients with Guillain-Barré syndrome and normal phrenic nerve conduction and normal diaphragmatic needle EMG, are unlikely to develop significant ventilatory failure.

The mean distal CMAP amplitude of limb nerves is reported to be a good predictor of outcome in Guillain-Barré syndrome.[17–19] In these reports the electrophysiological results were not correlated with the requirement for ventilation. In our study the thenar CMAP amplitude correlated with the need for ventilation, and the correlation was even stronger for phrenic nerve conduction.

In conclusion, we recommend that phrenic nerve conduction studies and diaphragmatic needle EMG be performed in the early stage of Guillain-Barré syndrome to detect patients who have respiratory muscle involvement and are at risk of respiratory decompensation.

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