Phrenic nerve CMAP amplitude, duration, and latency could predict respiratory failure in Guillain-Barré syndrome

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ABSTRACT

الأهداف: التحقق من نسبة انتشار اضطرابات العصب الحُجابي لدى مرضى متلازمة غيلان بارية، بالإضافة إلى تقييم دور دراسة حالة العصب الحُجابي في التنبؤ بحدوث الفشل التنفسي.

الطريقة: أُجريت هذه الدراسة خلال عام واحد من يوليو 2008م إلى يوليو 2009م، وشملت 28 مريضاً مصاباً بمتلازمة غيلان باريه ممن دخلوا إلى مستشفى الزهراء التابع لجامعة أصفهان للعلوم الطبية، أصفهان، إيران. لقد قمنا باستثناء المرضى الذين ظهرت عليهم العوامل المهيئة للأمراض التالية: السكري، وقصور الدرقية، واليوريميا، ونقص الفيتامينات، والتسمم. وقمنا بدراسة العصب الحُجابي في الأسبوع الأول بعد بداية ظهور الأعراض وذلك اعتماداً على وصف بيرستون وشابيرو.

النتائج: أشارت نتائج الدراسة إلى وجود اختلاف كبير من الناحية الإحصائية بين مرضى متلازمة غيلان باريه الذين يشكون من الفشل التنفسي وهؤلاء الذين لا يشكون من الفشل التنفسي وذلك من ناحية التالي: كمون إمكانية حركة عضلات التنفس البطني، ومدى كمون إمكانية حركة عضلات التنفس البطني الأيمن، وفترة كمون إمكانية حركة عضلات التنفس البطني. ولقد كانت فترة كمون إمكانية حركة عضلات التنفس البطني لدى مرضى متلازمة غيلان باريه الذين يشكون من الفشل التنفسي أطول من الفترة التي حصلت عليها مجموعة الشاهد (p=0.018)، واجتياز هذه الفترة للحد 9.6 كان كمنبه لإمكانية معاناة مرضى متلازمة غيلان بارية من الفشل التنفسي.

خاتمة: أثبتت الدراسة بأن التنبؤ بإمكانية حدوث الفشل التنفسي لدى مرضى متلازمة غيلان باريه لا يقتصر فحسب على كمون ومدى كمون إمكانية حركة عضلات التنفس البطني بل يمكن التنبؤ بهذه المشكلة اعتماداً على طول فترة كمون إمكانية حركة عضلات التنفس البطني.

Objectives: To determine the frequency of phrenic nerve abnormalities in Guillain-Barré syndrome (GBS), and evaluate the value of phrenic nerve conduction studies in predicting ventilation failure.

Methods: During a study period of one year between July 2008 and July 2009, 28 GBS patients referred to our tertiary university hospital (Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran) were enrolled in a case control study. Patients with predisposing factors for other polyneuropathies (diabetes mellitus, hypothyroidism, uremia, vitamin deficiency and toxicity) were excluded from the study. Phrenic nerve conduction was studied in the first week after the beginning of symptoms according to the procedure described by Preston and Shapiro.

Results: Diaphragmatic compound muscle action potential (CMAP) latencies, right diaphragmatic CMAP amplitude, and diaphragmatic CMAP duration were significantly different between GBS patients with respiratory failure and without respiratory failure. The CMAP duration was longer in GBS patients with respiratory failure than in the control group (p=0.018), and a CMAP duration of more than 9.6 is an alarm for impending respiratory failure in GBS patients.

Conclusion: Not only phrenic nerve CMAP latency and amplitude, but also diaphragmatic CMAP duration could have predictive value for respiratory failure in GBS patients.

Neurosciences 2012; Vol. 17 (1): 57-60

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Received 31st July 2011. Accepted 28th November 2011.

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Disclosure. The authors declare no conflict of interest, and were not supported or funded by any drug company.

Guillain-Barré syndrome (GBS) is an immune-mediated polyneuropathy, generally presenting with motor, sensory, and autonomic symptoms. Patients usually present with an acute inflammatory demyelinating polyneuropathy characterized by progressive muscle paralysis and reduced or absent reflexes with or without sensory or autonomic dysfunction; however, variants affecting cranial nerves or pure motor involvement are also described.[1] In severe cases, a combination of multiple clinical factors[2] culminate in neuromuscular respiratory failure in up to 30% of the patients.[3-7] The classical signs of respiratory distress occur too late,[8] and detection of primary signs of respiratory dysfunction is of significant importance in the management of GBS.[9] When both halves of the diaphragm are paralyzed, evaluation of diaphragmatic movements by fluoroscopy is not very informative and vital capacity measurement is not sensitive enough, particularly early in the course of the illness.[10] Davis[11] described a simple method of phrenic nerve conduction study in humans. He proposed that the phrenic nerve 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. Theoretically phrenic nerve conduction studies could be used as a marker of respiratory muscle weakness.[12,13] Therefore, the present work was designed to determine the frequency of phrenic nerve abnormalities in GBS, and also to evaluate the value of phrenic nerve conduction studies in predicting ventilation failure.

Methods. During a study period of one year between July 2008 and July 2009, 28 GBS patients (three male and one female patient with respiratory failure, and 14 male, and 10 female patients without respiratory insufficiency) referred to our tertiary university hospital (Alzahra hospital, Isfahan University of Medical Sciences, Isfahan, Iran) were examined. The diagnosis was based on the criteria suggested by Masucci and Kurtzke,[14] and confirmed in all patients by appropriate electro-diagnostic (EDX) tests. Inclusion criteria were acute limb paralysis and hyporeflexia, and confirmation of acute polyneuropathy in EDX studies. Patients with predisposing factors for other polyneuropathies (diabetes mellitus, hypothyroidism, uremia, vitamin deficiency and toxicity) were excluded from the study. The GBS patients with respiratory failure, which was defined as need for intubation and assisted ventilation, comprised the case group, and those without respiratory failure comprised the control group.

Phrenic nerve conduction was studied in the first week after the beginning of symptoms according to the procedure described by Preston and Shapiro.[15] The patient lay supine with the head slightly extended and rotated to the opposite side of 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 sternocleidomastoid and 3 cm above the clavicle. Surface recording electrodes were placed 16 cm apart with G1 (active electrode) 2 fingers above the xiphoid process, and G2 (reference electrode) on the anterior costal margin. The ground electrode was attached over the anterior chest wall. The latency of the diaphragmatic compound muscle action potential (CMAP) was measured from the stimulus artifact to the onset of the potential. The duration and the peak to peak amplitude of the diaphragmatic CMAP were also determined.

Data were collected using nerve conduction study tables, and a designed questionnaire was completed by one of the investigators and rechecked by another investigator. The gathered data were entered into the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA) software and analyzed using t-test and Mann Whitney test. *P*-values and confidence intervals were determined, and the ROC curve was used for calculation of cut points. Ethical approval to conduct this study was obtained from the ethics committee of Isfahan University of Medical Sciences.

Results. Seventeen males and 11 females in the age range of 11-72 years in the case group, and 17-76 years in control group were recruited, and phrenic nerve conduction studies were performed in all of them. Four patients (14%) developed respiratory failure (case group). The mean right diaphragmatic CMAP latency was 10.92 (5.31) ms in the case group, and 7.80 (2.10) ms in the control group. The mean left diaphragmatic CMAP latency was 12.30 (7.60) ms in the case group, and 8.00 (2.26) ms in the control group. The right (p=0.02) and left (p=0.01) diaphragmatic CMAP latencies in patients with respiratory failure were significantly more prolonged than in the control patients. The mean right and left diaphragmatic CMAP latency in patients with respiratory failure was significantly more prolonged than in the control patients (p=0.01) (**Table 1**). The mean right diaphragmatic CMAP amplitude was 0.20 (0.08) mv in the case group, and 0.37 (0.18) mv in the control group. The mean left diaphragmatic CMAP amplitude was 0.23 (0.19) mv in the case group, and 0.42 (0.24) in the control group. The right diaphragmatic CMAP amplitude was significantly lower in the case group than in the control group (p=0.03), but this difference was not significant on the left side (p=0.07). The mean right and left diaphragmatic CMAP amplitude was significantly higher in the control group (p=0.03). The mean diaphragmatic CMAP duration was 12.43 (6.01) ms in

Table 1 - Comparison of mean latency, amplitude, and duration of compound muscle action potentials in the phrenic nerve of case and control patients.

Value	Minimum		Maximum		Mean		SD		*P*-value
	Case	Control	Case	Control	Case	Control	Case	Control	
Rt CMAP latency (ms)	6.45	5.50	18.6	16.25	10.92	7.80	5.31	2.10	0.02
Lt CMAP latency (ms)	5.75	5.55	23.15	14.10	12.30	8.00	7.60	2.26	0.01
Rt CMAP amplitude (mv)	0.10	0.10	0.30	0.80	0.20	0.37	0.08	0.18	0.03
Lt CMAP amplitude (mv)	0.10	0.10	0.50	1.00	0.23	0.42	0.19	0.24	0.07
Mean CMAP latencies of Rt and Lt	6.10	5.35	20.88	14.00	11.60	7.90	6.43	2.01	0.01
Mean CMAP amplitude of Rt and Lt	0.10	0.10	0.40	0.85	0.21	0.39	0.13	0.18	0.03
CMAP duration (ms)	7.10	4.95	21.00	15.20	12.43	8.44	6.01	2.80	0.018

Rt - right, Lt - left, CMAP - compound muscle action potential, SD - standard deviation

the case group, and 8.44 (2.8) ms in the control group. The diaphragmatic CMAP duration was significantly longer in the case group (p=0.018). According to the ROC curve, the cut points of different quantitative values of the phrenic nerve for determination of respiratory failure were determined. The cut point of the right diaphragmatic CMAP latency was 8.67 with sensitivity of 75% and specificity of 83%. The cut point of the left diaphragmatic CMAP latency was 8.85 with sensitivity of 75% and specificity of 79%. The cut point of the mean left and right diaphragmatic CMAP latency was 8.78 with sensitivity of 75% and specificity of 83%. The cut point of diaphragmatic CMAP duration was 9.6 with sensitivity of 75% and specificity of 80%.

Discussion. More than 20-30% of GBS patients succumb due to ventilatory failure.[3,4] Early recognition, and timely institution of appropriate measures result in considerable reduction of mortality.[3,4,13] Clinical assessment and vital capacity measurements, though useful, are not sensitive enough to detect ventilation failure in the early stages.

Only a few studies investigated the electrophysiology of the phrenic nerve in respiratory failure.[16] In Ito et al's study,[17] clinical assessment was not correlated with phrenic nerve conduction or subsequent respiratory failure; but, phrenic nerve conduction studies were proportional to measurements of respiratory functions such as vital capacity. They suggested that, not only delayed distal latency, but also decreased amplitude of the phrenic nerve during the early stage of GBS may predict the need for respiratory assistance during the subsequent disease course.

From Bolton's study,[18] and the report of another study,[19] it is estimated that phrenic nerve conduction studies could provide one of the earliest indications of involvement of respiratory muscles in lower motor neuron disorders, and in most instances herald respiratory insufficiency. In clinical practice, these parameters could be used to advantage in the selection of patients who might require respiratory assistance in the future. In the present study, only 14% of patients developed respiratory failure and in this group phrenic nerve conduction time was significantly more prolonged than in those without respiratory failure. In a French study conducted by Durand et al,[20] the amplitude and latency of diaphragmatic CMAP were measured. Both variables were correlated with vital capacity (VC) but were similar in unventilated (n=60) and ventilated (n=10) patients. In Zifco and colleagues' study,[21] the phrenic nerve conduction measurement was measured in 40 GBS patients, and more parameters of the phrenic nerve study were recorded. The onset latency, amplitude, duration, and area of the diaphragmatic CMAP were abnormal in 83% of the patients. They concluded that the diaphragmatic CMAP amplitude (p=0.005), and area (p=0.001) were correlated with the need for ventilation, but diaphragmatic CMAP latency or duration had no predictive value.

In our study, although the number of patients in the case group was small, the results between the case and control groups were different enough to be statistically meaningful. The phrenic nerve CMAP latencies were significantly prolonged in the case group, and reduction in the mean amplitude of the right and left phrenic nerves was related to respiratory failure in GBS patients. In addition, in contrast to Zifco's study,[21] our results demonstrated that the CMAP duration was longer in GBS patients with respiratory failure than in the control group (p=0.018), and a CMAP duration of more than 9.6 is an alarm for impending respiratory failure in GBS patients.

The limitation of our study was the small number of patients who developed respiratory failure, and despite the fact that our results were statistically meaningful, reproduction of the study with a larger number of patients will confirm the results.

We conclude that not only phrenic nerve CMAP latency and amplitude, but also diaphragmatic CMAP duration could have predictive value for respiratory failure in GBS patients.

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