SINGLE FIBER ELECTROMYOGRAPHY IN ORBICULARIS OCULI AND FRONTALIS: RELATIVE SENSITIVITY IN MYASTHENIA GRAVIS

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Abstract

Objectives: The sensitivity of Single Fiber Electromyogram for the diagnosis of neuromuscular transmission disorders is high. The facial muscles usually tested are Orbicularis oculi and Frontalis. In this study we investigated the relative sensitivity of these two muscles in myasthenia gravis

Methods: The patients are divided in 3 groups: Patients with ocular symptoms (ptosis and/or diplopia) (group 1), with bulbar and/or limb weakness (group 2) and in clinical remission (group3). SFEMG was performed with a concentric needle electrode using voluntary activation. Mean consecutive difference and upper normal values for individual fiber pairs are compared with our normal values

Results: A total of 51 consecutive myasthenia gravis patients are recruited: 22 male and 29 female, mean age 56.3±17.3 years. The sensitivity of Orbicularis oculi is found 76.9 and of Frontalis 68.6. Combining the two muscles, their sensitivity reaches 86.5%. Both muscles are found more frequently abnormal in group 2. In group 1 we observed significantly more frequently abnormal jitter values in those with both ptosis and diplopia.

Discussion: Both facial muscles show high sensitivity in the diagnosis of Myasthenia gravis and both are complementary in the diagnosis of neuromuscular junction diseases. We propose Orbicularis oculi as the first muscle to be tested.

Key words: Single fiber Electromyogram, Myasthenia gravis, Orbicularis oculi, Frontalis

Η ΕΥΑΙΣΘΗΣΙΑ ΤΟΥ ΗΛΕΚΤΡΟΜΥΟΓΡΑΦΗΜΑΤΟΣ ΜΟΝΗΡΟΥΣ ΜΥΙΚΗΣ ΙΝΑΣ ΣΤΟ ΣΦΙΓΚΤΗΡΑ ΤΩΝ ΒΛΕΦΑΡΩΝ ΚΑΙ ΣΤΟ ΜΕΤΩΠΙΑΙΟ ΣΤΗ ΔΙΑΓΝΩΣΗ ΤΗΣ ΜΥΑΣΘΕΝΕΙΑΣ

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Περίληψη

Εισαγωγή: Η ευαισθησία του ηλεκτρομυογραφήματος μονήρους μυικής ίνας στη διάγνωση των διαταραχών της λειτουργίας της νευρομυικής σύναψης είναι υψηλή. Οι μυς του προσώπου οι οποίοι συνήθως ελέγχονται είναι ο Σφιγκτήρας των βλεφάρων και ο Μετωπιαίος. Σε αυτή τη μελέτη συγκρίναμε την ευαισθησία της εξέτασης των δύο αυτών μυών στη μυασθένεια.

Υλικό-Μέθοδος: Οι ασθενείς χωρίστηκαν σε 3 ομάδες: Ασθενείς με οφθαλμικά συμπτώματα (πτώσις βλεφάρωνή/και διπλωπία) (1η ομάδα), με προμηκικά συμπτώματα ή/και αδυναμία άκρων (2η ομάδα), ασθενείς σε κλινική ύφεση (3η ομάδα). Η εξέτασις έγινε με ομόκεντρο βελονοειδές ηλεκτρόδιο με εκούσια σύσπαση.Ο μέσος όρος συνεχόμενης διαφοράς (MCD) και η ανώτερη φυσιολογική τιμή για κάθε ζεύγος ινών συγκρίθηκαν με τις φυσιολογικές τιμές του εργαστηρίου μας.

Αποτελέσματα: Στη μελέτη περιελήφθησαν 51 ασθενείς με τη σειρά εμφάνισης στο εργαστήριο, 22 άνδρες και 29 γυναίκες μέσης ηλικίας 56,3±17,3 ετών. Η ευαισθησία του Σφιγκτήρα των βλεφάρων ήταν 76,9 και του Μετωπιαίου 68,6. Σε συνδυασμό των δύο μυών η ευαισθησία ήταν 86,5. Η ευαισθησία και των δύο ήταν μεγαλύτερη στη 2η ομάδα. Στην 1η ομάδα η ευαισθησία ήταν μεγαλύτερη στους ασθενείς με πτώση βλεφάρων και διπλωπία.

Συζήτηση: Και οι δύο μυς έδειξαν υψηλή ευαισθησία στη διάγνωση της μυασθένειας. Και οι δύο είναι συμπληρωματικοί στη διάγνωση των διαταραχών της λειτουργίας της νευρομυικής σύναψης. Προτείνουμε το Σφιγκτήρα των βλεφάρων σαν τον πρώτο μυ για το Ηλεκτρομυογράφημα μονήρους μυικής ίνας.

Λέξεις- κλειδιά: Μυασθένεια, Ηλεκτορμυογράφημα μονήρους μυικής ίνας, σφιγκτήρας βλεφάρων, μετωπιαίος

Introduction:

Single fiber Electromyography (SFEMG) is the most sensitive method for evaluating neuromuscular transmission among all the diagnostic tests when performed in a weak muscle: Sensitivity 75%-98% for generalized myasthenia gravis (GMG) and 62%-100% for ocular (OMG) and approximately with the same specificity [1-5] Orbicularis oculi (OOc) and Frontalis (Fr) are the muscles usually tested in patients with suspected MG and ocular symptoms (ptosis and/or diplopia). As far as we know, there are only a few studies comparing the relative sensitivity of these two muscles [6-7]

In this study we checked SFEMG relative sensitivity of OOc and Fr in myasthenia gravis (MG) patients.

Material and methods:

Consecutive patients with myasthenia gravis were included prospectively in the study. The diagnosis of MG was definite and was based on the following criteria: Symptoms of fluctuating muscle weakness and objective weakness on clinical examination and one of the following: 1. Elevated acetylcholine receptor (AchR) antibodies or antibodies to muscle-specific tyrosine kinase (MuSK). 2. Abnormal single-fiber electromyogram (SFEMG) in one muscle. 3. Abnormal repetitive nerve stimulation (RNS) in at least one symptomatic muscle (minimum 10% decrement in the compound muscle action potential amplitude). 4. Response to pyridostigmine therapy.

The patients were divided in 3 groups: Patients with ocular symptoms (ptosis and/or diplopia) (group 1), with bulbar and/or limb weakness (group 2) and asymptomatic, in clinical remission (group3).

For the electrophysiological study a Keypoint NET, Medtronic, Skovlunde, Denmark apparatus was used. SFEMG was performed with a concentric needle electrode 0.3 mm diameter,30 Gauss (Alpine biomed Aps Skovlunde Denmark) using voluntary activation. Amplifier filters 500Hz-10KHz, sweep velocity 1ms/div and amplitude 200 μV/div. For each pair 50 -100 traces were recorded for analysis and 20 pairs were obtained from each muscle. Acceptable pairs were those with amplitude of at least 50μV and rise time less than 300μs. Jitter was considered abnormal when 1. Mean consecutive difference (MCD) exceeded our normal values for each muscle (OOc > 27.2 μs, Fr > 29.8 μs). 2. More than 2/20 pairs MCD exceeded our upper normal values for individual fiber pairs (OOc > 38.7μs, Fr >42.1 μs) [9]. 3. When blocking was present in at least 1/20 pairs [10]. jitter value less than 5μs were non accepted [11]. The criteria for accepted waveforms proposed from Stalberg et al [12] are adopted.

Anticholinesterase medication was withheld 12 h prior to testing and skin temperature was maintained between 32-34°C. Written informed consent was obtained from participants and the study was approved from our local ethics committee (319/ 2/6/2017).

Descriptive statistics were used for quantitative presentation of the variables. 2 x 2 or 3 x 2 contingency tables were employed in order to test for frequency dependencies in categorical variables by means of Pearson's chi-squared tests. This analysis was also applied to the 3 x 2 matrix of the "MG-symptoms x SFEMG result" table, which was based on a rather small sample of muscles. Despite the fact that chi-square statistics may yield less consistent results with such small samples, it was not feasible to employ Fisher's exact test, since the latter is only indicated in 2 x 2 matrices. Finally, Cohen's kappa statistic was used to investigate the agreement between OOc and Fr SFEMG results. Significance was set at 0.05.

Results: The demographic characteristics of the study population are shown in table1. A total of 51 patients were tested: 22 male and 29 female, mean age 56.3±17.3 years (range 14-81). AchR antibodies positive were 37 patients (72.6 %), MuSK antibodies positive were 4 (7.8%) and seronegative 10 (19.6%), 9 of which had abnormal jitter in OOc and/or in Fr and one had fluctuating ocular symptoms (ptosis) compatible with MG and response to therapy.

In group 1 were included 26 patients, 17 in group 2 and 8 in group 3. Both muscles are found more frequently abnormal in group 2 (P< 0.01). The sensitivity of OOc is found 76.6%, of Fr 68.6% and combining the two muscles, their sensitivity reaches 86.5% (Table 1). A slight but not significant superiority of OOc versus Fr is noted in subgroups.

In group 1 abnormal jitter in OOc was observed in 10 out of 12 patients with both diplopia and ptosis (83.3%), and in Fr in 6 (50%) (P< 0.01). Of the 10 patients with ptosis, jitter in OOc was abnormal in 5 patients (50%) and in Fr in 6 (60%). There were 4 patients with diplopia, and jitter in OOc was abnormal in all 3 (75%) and in Fr in 2 (50%). In all 3 patients with MuSK antibodies, jitter was abnormal in both muscles.

In group 3 we found abnormal jitter in OOc in 62.5% and in Fr in 50% and in combination of the two muscles 87.5%.

Kappa agreement between OOc and Fr was 0.321 (fair agreement), p<0.05.

Table 1. Demographic data of the 51 patients and abnormal jitter in the subgroups of MG

Age mean, SD, (Range)		56.3±17.3 (17-81)				
Abs n, (%)		Ach 37(72.5)	MuSK 4 (7.8)	Seronegative 10 (19.6)		
Sex, n		Male=22	Female=29			
Abnormal jitter, n, (%)	**Total** n=44 (86.3)	**Ocular MG** 26 (51)	**Generalized MG** 17 (33,3)	**In Clinical remission** 8 (15.7)	**P value**	**Sensitivity**
OOc n, (%)	39(76.5)	17 (65.4)	17 (100)	5 (62.5)	<0.001	76.5%
Fr. n, (%)	35(68.6)	15 (57.7)	16 (94.1)	4 (50)	<0.001	68.6%
OO + Front n, (%)	30(58.8)	11 (42.3)	16 (94.1)	3 (37.5)	<0.001	86.5%

Fr=Frontalis, OO= Orbicularis oculi

Discussion:

We prospectively investigated jitter relative sensitivity of two facial muscles in MG patients: OOc. and Fr. These muscles are those more frequently investigated, especially in OMG and their sensitivity, alone or in combination, is found 70-100% [3-8]. More studies compare one facial muscle with extensor digitorum communis.

Relative sensitivity of the two facial muscles is reported in a few studies. Valls canals et al [6] found SFEMG of the OOc more sensitive for the diagnosis of OMG than of Fr. Coumouydjian et al [7] reported Fr slightly more sensitive than OOc.

In this study we could not find any statistically significant difference between the two muscles, although a slight superiority of OOc is noted in all subgroups of MG patients.

Both muscles were found more frequently abnormal in GMG than in OMG and this is noted in previous also studies. Abraham [13] reported that higher jitter (>100 ls) and higher decrement (>10%) values in RNS were more frequent in GMG. Koumouydjian et al [7] found OOc being most abnormal in GMG and Fr in OMG and combining the two muscles, jitter was slightly more abnormal in OMG than in GMG (100% versus 92.9%). Morren et al [5] found SFEMG sensitivity 73% in OMG and 85% in GMG. Sanders and Howard [2] also found more abnormal jitter in GMG than in OMG (86-100% versus 78%). Jitter is also frequently abnormal in patients in clinical remission. Sanders and Howard [2] found abnormal jitter values in facial muscles in 64% of their patients in clinical remission.

In the subgroup of patients with ocular symptoms we observed significantly more frequently abnormal jitter values in those with both ptosis and diplopia than in those with ptosis only and OOc significantly more abnormal in the patients with ptosis and diplopia, while Fr is found slightly more abnormal in those with ptosis only. Our previous study [14] and also the study of Batocchi et al [15] have shown that the presence of both diplopia and ptosis is more likely due to MG rather than to other diseases. Abraham et al [13] showed that MG patients with higher jitter values in Fr more frequently had a combination of ptosis and impaired extraocular movements. Mittal et al [16] also noted that patients with OMG who were transformed to GMG were those with both diplopia and ptosis, and no one with isolated ptosis or diplopia.

SFEMG is the most sensitive electrodiagnostic test for the diagnosis of MG, but it requires experienced personnel and patient cooperation. In this study we found high sensitivity of jitter (94-100%) for both muscles in GMG and significantly lower in the other two groups. As shown with Cohen's Kappa agreement between OOc and Fr, both muscles are complementary in the diagnosis of MG and we propose OOc as the first muscle to be tested in both OMG and GMG.

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