Journal of Neurological Sciences [Turkish] **34:(3)**# 59; 207-214, 2017
http://www.jns.dergisi.org/text.php3?id=1053
doi: 10.24165/jns.10168.17
Research Article

Jitter Measurement using a Concentric Needle in 133 Patients with Myasthenia Gravis: A Retrospective Analysis

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Summary

Objectives: Single-fiber electromyography is being used in the diagnosis of patients with myasthenia gravis (MG) and is more sensitive, although less specific, than repetitive nerve stimulation (RNS). For the past two decades, concentric needle electrodes (CN) have been used in calculating jitter. In this retrospective study, we aimed to reveal the sensitivity of CN-jitter in patients with MG.
Methods: Patients with MG who were followed up in our neuromuscular clinic were recruited to the study. Clinical findings and CN-jitter analyses were reviewed retrospectively.
Results: Among the 401 patients with MG who were admitted to our neuromuscular clinic, 155 patients were investigated electrophysiologically. Among them, 136 patients underwent CN-jitter analysis. Eighty-four percent of the patients had high jitter. The sensitivity of CN-jitter was 80% when only one muscle was studied, whereas the sensitivity rose to 90% when two muscles were studied. The sensitivity of CN-jitter in ocular MG (OMG) and generalized MG (GMG) was 81% and 86%, respectively. MuSK-ab positive patients tended to have the highest positivity in CN-jitter (92%), followed by AChR-ab positive (86%) and seronegative patients (75%). Twenty-five of 26 patients with GMG had positive CN-jitter in the extensor digitorum communis (ED) muscle.
Conclusion: CN-jitter is a sensitive method in patients with MG. Sensitivity improved when two muscles were studied.

Key words: Jitter, concentric needle electrode, myasthenia gravis, single-fiber electromyography

Özet

Amaclar: Tek lif EMG miyastenia gravis (MG)'li hastaların tanısında kullanılmaktadır, repetitif sinir stimulasyonuna kıyasla daha ay spesifik olmasına ragmen daha duyarlıdır. Gectiğimiz iki dekad boyunca konsantrik igne elektodlari (CN) jitter hesaplanmasında kullanılmıştır. Bu retrospektif çalışmada, MG hastalarında CN-jitterin duyarlılığını ortaya koymayı hedefledik**.**
Yontem: Noromüsküler klinigimizde izlenen MG tanılı hastalar çalışmaya dahil edildi. Klinik bulgular ve CN-jitter analizleri retrospektif olarak analiz edildi.
Sonuçlar: Nöromüskuler kliniğimize başvuran MG tanılı 401 hastanın arasında 155'i elektrofizyolojik olarak incelendi. Aralarında 136 hastaya CN jitter analizi yapıldı. Hastaların % 84'ünün yüksek jitteri vardı. CN jitter duyarlılığı bir kas çalışıldığında % 80 bulundu, iki kas çalışıldığında ise duyarlılık % 90'a yükseldi. Okuler MG'de (OMG) ve jeneralize MG'de (GMG) CN-jitter in duyarlılığı sırasıyla % 81 ve % 86 idi. Musk –AB pozitif hastaların CN-

jitter pozitivitesi en yüksekti (% 92), bunu AchR-ab pozitif (% 86) ve seronegatif (% 75) hastalar izliyordu. GMG'li 26 hastanın 25'inde ekstensör digitorum kommunis kasında pozitif CN-jitteri bulundu.
Sonuçlar: CN-jitteri MG'li hastalarda duyarlı bir yöntemdir. Duyarlılık iki kas çalışıldığında artmaktadır.

Anahtar Kelimeler: Jitter, konsantrik iğne elektrodu, miyastenia gravis, tek lif elektromiyografi

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder characterized by fluctuating muscle weakness. Electrophysiologic studies such as repetitive nerve stimulation (RNS) and single-fiber electromyography (SFEMG) are important in the diagnosis of this disease.

In generalized MG (GMG), the sensitivity of RNS increased to 87% when proximally located muscles and periocular/facial muscles were studied (1-4). In ocular MG (OMG), the sensitivity of RNS was low (17-45%) compared with GMG (2,4,5).

SFEMG is the most sensitive diagnostic test in patients with MG. High jitter was found in 86% of patients with GMG when the extensor digitorum communis (ED) muscle was studied; it was 92% when one periocular muscle (frontalis or OOc) was added to the study and 99% when a third was added (6).

In late 1990s, disposable concentric needle electrodes (CN) were proposed for use in jitter measurements in the diagnosis of MG (7,8). CN-jitter analysis was shown to have equal sensitivity to SFEMG in the diagnosis of MG (7,9-11). The aim of this retrospective study was to calculate the diagnostic sensitivity of CN-jitter in patients with MG.

MATERIAL AND METHODS

Patients with MG who were followed up in our neuromuscular disease outpatient clinic (Department of Neurology, Istanbul Faculty of Medicine, Istanbul University) between January 2009 and August 2014 were evaluated retrospectively. The diagnostic criteria for MG were fluctuating weakness, and at least one of the following: 1) response to anticholinesterase treatment, 2) positive acetylcholine receptor or muscle-specific kinase antibody test.

The electrophysiologic examinations were evaluated from the patients" files and the EMG archive. CN-jitter studies were performed during voluntary contraction with either 25 mm or 37 mm CN with a large recording surface (0.07 mm2). The high-pass filter (HPF) was set to 2 kHz. The study was accepted as abnormal when more than 10% of the recorded potentials revealed high individual jitter (?55 µs) and/or the mean jitter value was high (?35 µs) according to the accepted reference values for SFEMG electrodes and/or there was blocking (12-14). The study was accepted as normal when at least 20 potential pairs were recorded and the criteria for an abnormal study (as mentioned above) were not met. Frontalis, orbicularis oculi (OOc), ED, or masseter muscles were used for CN-jitter analysis. The physician who examined the patient decided which muscle was to be chosen for CN-jitter. The patients were accepted as having OMG when the symptoms were limited to the ocular muscles for more than 2 years (15). Istanbul University Istanbul Faculty of Medicine Ethics Committee approved the study (2014/1617, 10.24.2014).

RESULTS

The total number of patients with MG seen in our neuromuscular clinic between January 2009 and August 2014 was 401. Among them, 156 patients were referred to

our EMG laboratory. The data of one patient were missing; therefore, a total of 155 patients" medical records were reevaluated. Of the 155 patients, 136 patients had CN-jitter; however, three were excluded because less than 20 potential pairs had been calculated. The remaining 133 patients" CN-jitter recordings were included in the study.

Frontalis, OOc, ED, and masseter muscles were used for CN-jitter (Table 1). Overall, 112 of 133 patients had high jitter (84%). In fifteen of the 21 patients with negative study, the jitter was measured in only one muscle (10 frontalis, 4 OOc, 1 ED). Fifty of the 112 patients with positive CN-jitter who had two or more muscles examined had high jitter in at least one muscle. Eighty-five of 112 patients with positive CN-jitter had a periocular muscle studied (76%). Nine of 47 (19%) patients OMG had normal CN-jitter, whereas 12 of 86 with GMG (14%) had normal studies (Table 1). The sensitivity of CN-jitter when only one muscle was studied was 80%, whereas the sensitivity rose to 90% when two muscles were studied. In 26 patients with GMG in whom ED only was studied, 25 had high jitter (96%). Twenty of 27 (74%) patients with OMG and 15 (68%) of 22 with GMG who had only one periocular muscle studied had high jitter. The relation between seropositivity and CN-jitter is shown in Table 2. High jitter in at least one muscle was observed in 93% of MuSK-ab positive patients, 86% of AChR-ab positive patients, and 75% of seronegative patients.

Table 1. Results of CN-jitter

CN-jitter	Positive (%)	Negative (%)
One muscle studied	61 (80.3)	15 (19.7)
Frontalis	29	10
OOc	6	4
ED	26	1
Two or more muscles studied	51 (89.5)	6 (10.5)
Two periocular (frontalis, OOc)	8	2
One periocular and ED	31	2
Periocular and masseter	3	2
Masseter and ED	1	-
Two periocular and masseter	1	-
Periocular, ED and masseter	7	-

Table 2. Sensitivity of CN-jitter according to MG subtypes

CN-jitter	Positive (%)	Negative (%)
Serology		
AChR-ab (+)	**65 (85.5)**	**11 (14.5)**
At least one periocular	*47*	*11*
ED only	*17*	-
ED and masseter	*1*	-
MuSK-ab (+)	**12 (92.3)**	**1 (7.7)**
At least one periocular	*8*	-
ED only	*4*	1
Seronegative	**18 (75)**	**6 (25)**
At least one periocular	*14*	*6*
ED only	*4*	-
AChR-ab (-)	**17 (85)**	**3 (15)**
At least one periocular	*1*	*3*
ED only	*16*	-
MG subtype		
OMG	**38 (80.9)**	**9 (19.1)**
At least one periocular	*37*	*9*
ED only	*1*	*0*
GMG	**74 (86)**	**12 (14)**
At least one periocular	*48*	*11*
ED only	*25*	*1*
ED and masseter	*1*	-

Seronegative: patients with a negative result of both AChR-ab and MuSK-ab analysis; AChR-ab (-): patients with only a negative result of AChR-ab analysis.

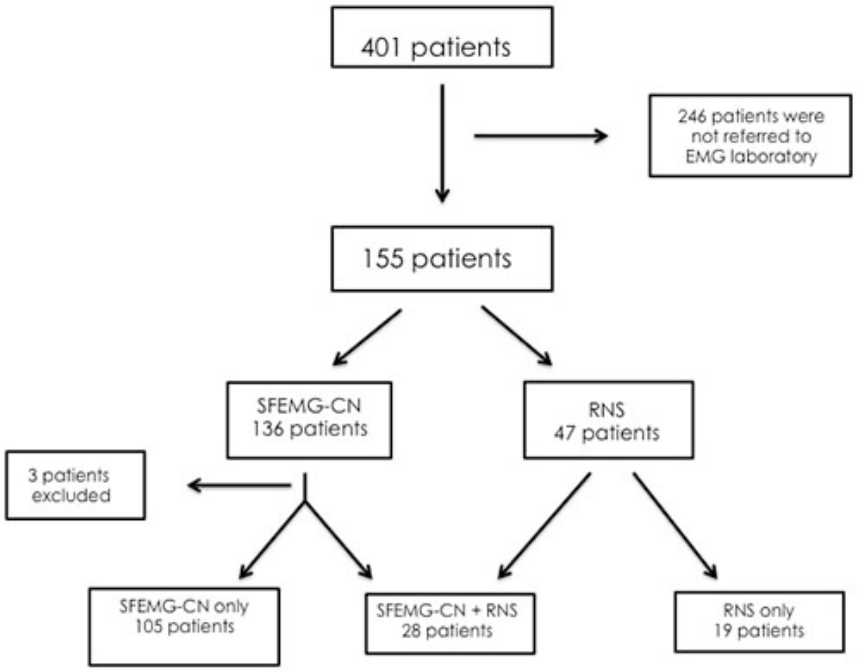

Figure 1: *Distribution of patients*

DISCUSSION

In this retrospective study, the sensitivity of CN-jitter was 85% in patients with MG. Our results were consistent with previous reports in which neuromuscular transmission was studied, either with single-fiber electrodes or CN (6,7,10,11,16).

In order to avoid blood-transmitted agents, high cost, and tiresome maintenance of single-fiber electrodes, CN is now recommended to calculate neuromuscular jitter for the diagnosis of MG. In order to be able to record a single fiber-like potential by CN, HPF should be raised to 1-2 kHz and a needle with a small recording surface should be used for selective recording (12,17,18).

The mean jitter values and number of abnormal jitters recorded using CN and SFEMG electrodes and the diagnostic sensitivity of jitter measurement by both electrodes in periocular and ED muscles for the diagnosis of MG were studied in various reports and no significant differences was found (7,10). In one study, the sensitivity of CN-jitter in the frontalis muscle was 67% and the specificity was 96% in patients with MG (5). Orhan et al. found the sensitivity of CN-jitter in GMG to be 95, 85, and 90% in periocular, ED, and masseter muscles, respectively (11).

In OMG, the sensitivity of SFEMG in the ED muscle was 63-80% in different reports (4,6). If a periocular muscle was added to the study, 88% of the patients had high

jitter (6). Costa et al. studied SFEMG in the OOc bilaterally in 15 patients with OMG and found abnormal jitter in each (19). In our study, 81% of patients with OMG had high jitter. To avoid overestimation, we preferred to use normative values described for single-fiber electrodes because the normal reference values of jitter analysis with CN were not known at the time of the measurements (13,14). This, in turn, could explain the relatively low sensitivity.

The reference values of neuromuscular jitter measured using CN were recently published (17). In their study, the HPF setting was raised to 1 kHz and a small needle with a recording surface of 0.019 μm2 was used. However, in our retrospective study, HPF was set to 2 kHz. It is now recommended to choose 1 kHz HPF setting in order to recognize summated signals and to avoid generating extra phases (17). Recently, Machado et al. showed that the sensitivity of CN-jitter was 92% in the OOc muscle for patients with OMG and 100% for patients with GMG when the 1 kHz HPF setting and new reference values were used (20). Our results are different from that study because the new reference values of individual and mean jitter for 1 kHz were lower than those previously used.

We found that the sensitivity of CN-jitter was slightly higher in the MuSK-ab positive group (92%) and lower in the seronegative group (75%) when compared with the AChR-ab positive group (86%). Oh et al. found the sensitivity of SFEMG in ED with single-fiber electrodes as 90% in the MuSK-ab positive group, 89% in the AChR-ab positive group, and 81% in the seronegative group (16). The reported sensitivity of CN-jitter was 94% in patients with MG who were AChR-ab positive when ED and OOc muscles were studied together with 2kHz HPF settings (9).

In our study, of the 26 patients with GMG whose ED muscle was the only muscle studied in CN-jitter, 25 (96%) had high jitter. In one patient with OMG, the ED, which was the only muscle studied, had high jitter. Seventy-four percent of these patients (20/27) were seropositive. Among the patients (n=106) in whom at least one periocular muscle was studied, 85 (80%) had high jitter. In patients with MG, the sensitivity of SFEMG increased from 86% to 99% if one periocular muscle was studied in addition to the ED muscle (6). We found that 86% (74/86) of patients with GMG had high jitter. The sensitivity of CN-jitter in ED muscles in GMG was similar to that in previous studies (4,6). The ED muscle is not recommended now because it is difficult to obtain appropriate signals (17). In our study, the physician who performed the EMG study chose muscles according to the clinical picture. The ratio of high jitter in the ED muscle could be explained by this biased selection of ED muscles in patients with more pronounced clinical findings.

The main limitation of this retrospective study was the lack of reference values for CN-jitter at 2 kHz HPF settings. In addition, examination protocols were different between the patients because the physician who performed the study decided which muscles should be studied for CN-jitter.

The other limitation of our study was the selection of patients. Instead of analyzing patients who were referred to our laboratory with a preliminary diagnosis of MG, we chose patients who were diagnosed as having MG and followed up at our neuromuscular outpatient clinic. Benatar et al. showed that the diagnostic sensitivity of CN-jitter in the frontalis muscle in MG was 67% when all patients who had CN-jitter analysis for suspicion of MG were recruited (5). Our results were higher than in this previous study because the patient selection was different.

CN-jitter is a sensitive method for the diagnosis of patients with MG. Periocular muscles seem to be reliable in jitter analysis. CN-jitter in the ED muscle can be

used in the diagnosis of GMG. The sensitivity became higher when two muscles were studied.

Author Contributions: Concept - N.G.Ş, E.K.O, H.D., P.O, Y.P, A.E.Ö, F.D, M.B.B; Design - N.G.Ş, E.K.O, H.D., P.O, Y.P, A.E.Ö, F.D, M.B.B; Supervision - N.G.Ş, E.K.O, M.B.B; Fundings - N.G.Ş, E.K.O, H.D., P.O, Y.P, A.E.Ö, F.D, M.B.B; Materials - N.G.Ş, E.K.O, M.B.B; Data Collection and/or Processing ; N.G.S, E.K.O; Analysis and/or Interpretation - N.G.Ş, E.K.O, M.B.B, F.D; Literature Search - N.G.Ş, M.B.B; Writing - N.G.Ş, E.K.O, H.D., P.O, Y.P, A.E.Ö, F.D, M.B.B; Critical Reviews - N.G.Ş, E.K.O, H.D., P.O, Y.P, A.E.Ö, F.D, M.B.B

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Received by: 08 April 2017
Revised by: 30 May 2017
Accepted: 30 May 2017

The Online Journal of Neurological Sciences (Turkish) 1984-2017
This e-journal is run by Ege University Faculty of Medicine,
Dept. of Neurological Surgery, Bornova, Izmir-35100TR
as part of the Ege Neurological Surgery World Wide Web service.
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E-mail: editor@jns.dergisi.org
URL: http://www.jns.dergisi.org
Journal of Neurological Sciences (Turkish)
Abbr: J. Neurol. Sci.[Turk]
ISSNe 1302-1664

REFERENCES

1. *Ozdemir C and Young RR. Electrical testing in myasthenia Gravis. Ann NY Acad Sci 1976; 274: 203-222.*
2. *Oh SJ, Eslami N, Nishihira T et al. Electrophysiological and clinical correlation in myasthenia gravis. Ann Neurol 1982; 12: 348,354.*
3. *Kelly JJ, Draube JR, Lennon VA, Howard FM, Younge BR. The laboratory diagnosis of mild myasthenia gravis. Ann Neurol 1982; 12: 238-242.*
4. *Oh SJ, Kim DE, Kuruoglu R, Bradley RJ, Dwyer D. Diagnostic sensitivity of the diagnostic laboratory tests in myasthenia gravis. Muscle Nerve 1992; 15: 720-724.*
5. *Benatar M, Hammad M, Doss-Riney H. Concentric-needle single-fiber electromyography for the diagnosis of myasthenia gravis. Muscle Nerve 2006; 34: 163-168.*
6. *Sanders DB and Howard JF. AAEE Minimonography 25: Single-fiber Electromyography in Myasthenia Gravis. Muscle Nerve 1986; 9: 809-819. <>7) Ertas M, Baslo MB, Yıldız N, Yazıcı J, Oge AE. Concentric needle electrode for neuromuscular jitter analysis. Muscle Nerve 2000; 23: 714-719.*
7. *Buchman AS, Garratt M. Determining neuromuscular jitter using a monopolar electrode. Muscle Nerve 1992; 15: 615-619.*
8. *Sarrigiannis PG, Kennett RP, Read S, Farrugia ME. Single-fiber EMG eith a concentric needle electrode: Validation in myasthenia gravis. Muscle Nerve 2006; 33: 61-65.*
9. *Farrugia ME, Weir A, Cleary M, Cooper S, Metcalfe R, Mallik A. Concentric and single fiber needle electrodes yield comparable jitter results in myasthenia gravis. Muscle Nerve 2009; 39: 579-585.*
10. *Orhan-Kocasoy E, Deymeer F, Oflazer P, Parman Y, Baslo MB. Jitter analysis with concentric needle electrode in the masseter muscle for the diagnosis of generalized myasthenia gravis. Clin Neurophysiol 2013; 124: 2272-2282.*
11. *Stålberg EV, Trontelj JV, Sanders DB. Single fiber electromyography studies in healthy and diseased muscle. 3rd Ed. Fiskebäckskil: Edshagen, 2010.*
12. *Gilchrist J, Barkhaus P, Bril V et al. Single fiber EMG reference values: a colloborative effort. Muscle Nerve 1992; 15: 151-161*
13. *Bromberg MB, Scott DM, and the Ad Hoc Committee of the AAEM single fiber special interest group. Single fiber EMG reference values: reformatted in tabular form. Muscle Nerve 1994; 17: 820-821.*
14. *Oh SJ, Morgan MB, Lu L et al. Different characteristic Phenotypes According to Antibody in Myasthenia Gravis. J Clin Neuromusc Dis 2012; 14: 57,65.*
15. *Oh SJ, Hatanaka Y, Hemmi S et al. Repetetive nerve stimulation of facial muscles in MuSK antibody-positive myasthenia gravis. Muscle Nerve 2006; 33: 500-504.*
16. *Stalberg E, Sanders DB, Ali S et al. Reference values for jitter recorded by concentric needle electrodes in healthy controls: A multicenter study. Muscle Nerve 2016; 53: 351?362.*

17. *Stalberg E. Jitter analysis with concentric needle electrodes. Ann NY Acad Sci 2012; 1274: 77-85.*
18. *Costa J, Evangelista T, Conceição I, de Carvalho M. Repetitive nerve stimulation in myasthenia gravis--relative sensitivity of different muscles. Clin Neurophysiol 2004; 115: 2776?2782.*
19. *Machado FCN, Kouyoumdjian JA, Marchiori PE. Diagnostic accuracy of concentric needle jitter in myasthenia: Prospective study. Muscle Nerve 2017; 55: 190-194.*