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Repetitive nerve stimulation test of the patients suspected of myasthenia gravis

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Objective : *To compare the test results of repetitive nerve stimulation to the final clinical diagnosis of patients who were suspected of myasthenia gravis.*

Setting : *Electrodiagnostic Laboratory, Department of Rehabilitation Medicine, Faculty of Medicine, Chulalongkorn University.*

Design : *Retrospective and descriptive study.*

Materials and Methods : *OPD cards and electro-diagnostic records of 100 patients who were suspected myasthenia gravis were reviewed on the results of repetitive nerve stimulation and their final clinical diagnosis. The percentage of the patients who had the same results of RNS and their final clinical diagnosis were calculated and analyzed. The measure of agreement, kappa reliability coefficient was also calculated by SPSS program.*

Results : *The most frequently found symptoms and signs of the patients were namely: ptosis, diplopia, generalized muscular weakness, dysphagia and dysarthria or dysphonia. The facial muscles (proximal muscle) were more frequently tested by RNS than the muscles of the forearm or the hand muscles (distal muscle). Other laboratory tests which clinicians used to confirm the final clinical*

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diagnosis were ice namely : ice test, thyroid hormone level, chest X-ray, CT- scan, pharmacological test and AchR antibody titer. Seventy-one percent of the patients had the same results of RNS test as the final clinical diagnosis. Furthermore twenty-four percent of ocular MG and seventy-two percent of generalized MG had abnormal response of RNS tests. The kappa reliability coefficient was 0.442.

Conclusion : *The results of repetitive nerve stimulation test had good agreement with clinicians' diagnosis in generalized MG but not good in ocular MG.*

Keywords : *Myasthenia gravis, Repetitive nerve stimulation.*

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วัตถุประสงค์ : *เพื่อเปรียบเทียบผลการตรวจไฟฟ้าวินิจฉัยด้วยวิธี repetitive nerve stimulation (RNS) กับผลการวินิจฉัยทางคลินิกของแพทย์ผู้ส่งตรวจว่ามีความสอดคล้องตรงกันมากน้อยเพียงใดในผู้ป่วยที่สงสัยว่าเป็นโรค myasthenia gravis*

รูปแบบการศึกษา : *การศึกษาเชิงพรรณนาชนิดย้อนหลัง*

สถานที่ทำการศึกษา : *ห้องตรวจไฟฟ้าวินิจฉัย ภาควิชาเวชศาสตร์ฟื้นฟู คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*

ประชากรที่ศึกษา : *ผู้ป่วยจำนวน 100 คน ที่ถูกส่งมาตรวจไฟฟ้าวินิจฉัยเพื่อช่วยวิเคราะห์แยกโรค myasthenia gravis ตั้งแต่ เดือนมกราคม 2543 ถึงเดือนธันวาคม 2545*

วิธีการศึกษา : *ศึกษาข้อมูลย้อนหลังทั้งในส่วนของผลการตรวจไฟฟ้าวินิจฉัยโดยวิธี RNS และผลการวินิจฉัยจากแพทย์ทางคลินิก จากเวชระเบียนของผู้ป่วย และศึกษาอาการสำคัญที่นำมา การส่งตรวจทางห้องปฏิบัติการอื่น ๆ กล้ามเนื้อที่ถูกตรวจด้วย RNS คำนวณหาร้อยละของผู้ป่วยที่มีผลการตรวจด้วย RNS และการวินิจฉัยทางคลินิกที่เหมือนกัน และคำนวณค่า kappa reliability coefficient โดยใช้โปรแกรมสำเร็จรูป SPSS*

ผลการศึกษา : *จากการศึกษาผู้ป่วยจำนวน 100 คนพบว่าอาการสำคัญที่นำผู้ป่วยมาพบแพทย์คือหนังตาตก เห็นภาพซ้อน กล้ามเนื้อแขนขาอ่อนแรง กลืนลำบาก เสียงแหบพูดไม่ชัด หายใจลำบาก และกล้ามเนื้อบริเวณใบหน้ากระตุก เรียงตามลำดับ ผู้ป่วยทั้งหมดได้รับการตรวจด้วย RNS โดยกล้ามเนื้อบริเวณใบหน้า ซึ่งจัดเป็นกล้ามเนื้อส่วนต้น (proximal muscle) มากกว่ากล้ามเนื้อบริเวณแขน และมือซึ่งจัดเป็นกล้ามเนื้อส่วนปลาย (distal muscle) การตรวจทางห้องปฏิบัติการอื่น ๆ ที่แพทย์ทางคลินิกใช้เพื่อช่วยในการวินิจฉัยโรค myasthenia gravis คือ ทดสอบด้วยน้ำแข็ง (ice test) ตรวจหาระดับฮอร์โมนไทรอยด์ เอ็กซเรย์ปอด เอ็กซเรย์คอมพิวเตอร์, ทดสอบด้วยยา (pharmacological test) และตรวจหาระดับ AchR antibody จากการเปรียบเทียบผลการตรวจด้วย RNS และการวินิจฉัยทางคลินิกพบว่าผู้ป่วยร้อยละ 71 มีผลการตรวจสอดคล้องกัน โดยมีค่า kappa reliability coefficient เท่ากับ 0.442 และพบว่าผู้ป่วยที่ได้รับการวินิจฉัยทางคลินิกว่าเป็น ocular MG มีผล RNS ผิดปกติร้อยละ 24 ส่วนในกลุ่มที่ได้รับการวินิจฉัยทางคลินิกว่าเป็น generalized MG มีผล RNS ผิดปกติร้อยละ 72*

สรุป : *ผลการตรวจไฟฟ้าวินิจฉัยด้วย RNS ตรงกับผลวินิจฉัยทางคลินิกโดยแพทย์ผู้ส่งตรวจสูงในกลุ่ม generalized MG แต่มีความตรงกันน้อยในกลุ่ม ocular MG*

Myasthenia gravis (MG) is an acquired autoimmune disorder of neuromuscular transmission resulted from deficient numbers of Acetyl Choline Receptors (AchRs). The clinical hallmark of MG is fluctuating skeletal muscle weakness worsened by repeated use and relieved by rest. [1-4] Complaints of weakness are usually limited to specific muscle groups, particularly the external ocular, various bulbar and proximal limb muscles. Diplopia and ptosis are the presenting symptoms and signs in about 50-90% of patients,[5] whereas others may present with dysarthria, dysphagia or weakness of proximal limbs. There is a significant association of the disease with pathology in the thymus gland. [6-7] Thymic hyperplasia mostly occurs in young patients and thymoma occurs approximately in 10 % of older male patients. There is an increased incidence of thyroid disease and other autoimmune condition in patients.[8]

The differential diagnosis of MG includes neuromuscular and non-neuromuscular conditions such as thyroid, eye disease, brain stem disease, mitochondrial myopathy, inflammatory myopathy, oculopharyngeal dystrophy, motor neuron disease and cranial nerve compression lesion. [9-11]

There is no gold standard of laboratory test for MG.[4] We can justly compare only the percent of the patients who demonstrate an abnormal result with various tests. The diagnostic methods which are commonly used to confirm MG are pharmacological test.[12] The two major electro-diagnosis tests for MG are repetitive nerve stimulation (RNS) and single fiber electromyography (SFEMG).

The electro-diagnosis laboratory of the Department of Rehabilitation Medicine, King Chulalongkorn Memorial Hospital has electro-diagnosis test in service for more than two decades, and the electro-diagnostic technique use to test for MG is repetitive nerve stimulation. Because we do not have any equipment for SFEMG. Many patients suspected of MG were referred to our lab from clinicians. But the statistic data about RNS results and final clinical diagnosis by referring doctor in these groups of patients have never been done; therefore we would like to find out the percentage of RNS results that were the same as those of clinicians diagnoses.

Objective

The goal of the study is to compare the results of repetitive nerve stimulation test to the final clinical diagnosis in patients who were suspected of myasthenia gravis.

Materials and methods

Methodologically, this study is a retrospective review of electro-diagnostic laboratory's records from January 2000 to December 2002, because the collected datas are available and complete. One hundred and twenty-five patients (average 41.67/year) were tested with RNS for confirming MG. But only one hundred patients (60 women and 40 men) whose OPD cards contained complete record of the symptoms and their final diagnosis were recruited into the study.

Repetitive Nerve Stimulation Test

For patients who were receiving anticholine-esterase medication (edrophonium or prostigmine), the medication was withdrawn for 12 hours before the examination. The guildlines for performing RNS are as follows:

1. Choose the proper tested muscle and

nerve. A surface active electrode is placed to the muscle's motor point while a reference electrode is located over the distal tendinous region.

2. Establish supramaximal CMAPs

3. Warm the tested muscle about 5 mins.

4. Stimulate nerve at 3 Hz for 10 responses. The percentage decrement is calculated by comparing the forth response with the first response. An amplitude decrement of more than 10 % is considered abnormal.

5. Repeat step B after several minutes of rest to ensure reproducibility.

6. Exercise muscle under investigation for:

A. If >10 % decrement present prier to exercise, look for facilitation and repair of decrement as well as postactivation exhaustion.

B. If no decrement present at rest, look for postactivation exhaustion Immediately after exercise, stimulate nerve at 3 Hz for 10 responses.

7. Repeat stimulation at 3Hz for 10 stimuli every 2 mins. For about 4 mins.

Result

One hundred records of patients (60 women and 40 men) were reviewed. The age of the patients ranged from 1 to 77 years. They were consulted by many specialties: 46 patients from neurologists, 46 patients from opthalmologists, 7 patients from internists, and 1 patient from a pediatrician. Ninety- eight patients were tested by RNS at proximal muscle (facial muscle), where as eighteen patients were tested at distal muscles (forearm or hand muscles). The most frequent complaints of the patients were, namely: ptosis, diplopia, generalized muscular weakness, dysphagia, dysarthria or dysphonia, dyspnea and facial muscle spasm, respectively. (Table 1)

Table 1. Initial presenting symptoms.

Symptoms	Number of patients
Ptosis	64
Diplopia	38
Generalized limb muscle weakness	23
Dysphagia	18
Dysarthria or dysphonia	13
Dyspnea	3
Facial muscle spasm	2
Other	3

The clinicians used both the characteristic symptoms and other laboratory tests to differentiate and confirm the diagnosis of MG. The laboratory testing which clinicians prescribed most frequently to the patients were ice test (all were prescribed by ophthalmologists), thyroid hormone level, chest X-ray or CT-scan (to rule out thymoma), pharmacologist test (tensilon test) and AchR antibody titer, respectively. (Table 2)

Table 2. The other laboratory testing which clinicians prescribed to the patients.

Test	Number of patients
Ice test	32
Thyroid hormone level	30
Chest X-ray or CT scan	26
Phamacological test	13
AchR antibody titer	1

The results of RNS test and the final clinical diagnosis are shown in Table 3. Among the one hundred patients, twenty-five had abnormal RNS result and seventy-five had normal RNS result. Where as fifty-four patients had final clinical diagnosis of MG and forty-six patients had a final clinical diagnosis of other diseases. On the basic of both results, three groups could be distinguished; the first group, of twenty-five patients had an abnormal RNS test with a final clinical diagnosis of MG; the second group of forty-six patients showed a normal RNS test and a final diagnosis of non-MG; the third group of twenty-nine patients had normal RNS test but a final clinical diagnosis of MG. There was no patients who had abnormal RNS test with a final diagnosis of non-MG. Comparing the clinical diagnosis to the result of RNS test, it was found that the results of seventy-one patients (71%)(Group 1 and 2) were on the same line with the diagnosis. Furthermore, it indicated that if the results of RNS were abnormal, the chance of being diagnosed of MG would be 100 %. And if the results of RNS were normal, the chance of being diagnosed of non-MG would be 61.33 %. The results of RNS test and final clinical diagnosis were statistically calculated for measuring agreement. The Kappa reliability coefficient was 0.442.

Table 3. Results of RNS test compare to the clinical diagnosis.

	Clinical diagnosis by the clinician		
Result of RNS test	**MG**	**Non-MG**	**Total**
Abnormal	25	0	25
Normal	29	46	75
Total	**54**	**46**	**100**

Fifty-four patients were clinical diagnosis of MG. They were devided in 2 groups. In the first group, twenty-nine patients were diagnosed of ocular MG and twenty-five patients in the second group were diagnosed of generalized MG. The results of RNS test in both groups are shown in Table 4. Seven patients (24 %) in the ocular MG group, had an abnormal RNS test; while eighteen patients (72 %) in the generalized MG group, had abnormal RNS test.

Discussion

The clinical presenting symptoms and signs of the patients who were suspected of MG and reffered for RNS test were, namely: ptosis, diplopia, generalized muscular weakness and dysarthria or dysphonia. This is similar to the findings of other previous studies.[4,5,8,13]

As for the RNS test in this study, ninety-eight percent were tested on the nasalis and the hand

Table 4. The results of RNS in ocular MG and generalized MG.

	Result of RNS		
Clinical diagnosis of MG	**RNS abnormal**	**RNS normal**	**Total**
Ocular MG	7	22	29
Generalized MG	18	7	25
Total	**25**	**29**	**54**

muscles. Because there were many clinical studies, which supported that the stimulation of a proximal muscle increases the percentage of abnormal responses of RNS test. [4,8,14,15]

It is difficult to define accurately the sensitivity and specificity of a particular test in the absence of the gold standard. As a result, one can justly compare only the percent of patients who demonstrate an abnormal result with various tests. The acceptable methods to diagnosis the myasthenia gravis are the electrophysiological test and the AchR antibody assay. The electro-physiological test includes both repetitive stimulation and SFEMG. But our hospital does not have both SFEMG and AchR antibody assay. So we can justly compare the result of repetitive stimulation with the clinicians' diagnosis. The percentage of patients who showed the same result of RNS test and their final clinical diagnosis was about 71 %. These patients divided into two group, the generalized MG and the ocular MG, the generalized MG patients had the abnormal RNS test 72 % more than 24% of ocular MG patients. When compare to other studies [13,16-19] that concluded the abnormality of RNS test in generalized MG and ocular MG were about 62-77 % and 45-50 % respectively. It was the same percentage in generalized MG but less percentage in ocular MG. The Kappa reliability coefficient only 0.442, showed that the result of RNS did not well agrees with the clinicians' diagnosis. So the further studies were needed to find the reason and improve the accuracy of RNS test especially in ocular MG patients.

Conclusion

The results of repetitive nerve stimulation test had good agreement with clinicians' diagnosis in generalized MG but not well in ocular MG.

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