Comparative Study of Diagnostic Significance of Urethral Sphincter Electromyography and External Anal Sphincter Electromyography in Patients with Multiple System Atrophy

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Abstract

Objectives: to evaluate the diagnostic value of external anal sphincter electromyography (EAS-EMG) and urethral sphincter electromyography (US-EMG) in patients with multiple system atrophy (MSA).

Methods: 35 patients who were diagnosed as MSA were examined as treatment group, while 53 non-MSA patients were examined as control group, using EAS and US-EMG. Data was recorded and analyzed, including spontaneous activities when relax, parameters of mean motor unit potential (MUP) duration and amplitude, MUP polyphasicity (percentage of polyphasic MUP) and variation when strong contraction.

Results: Neurogenic injury was showed in US-EMG and EAS-EMG in 27 cases of MSA group (77.1%). There were significant differences for MUP duration between MSA and non-MSA cases by both EAS-EMG (t=3.515, P=0.001) and US-EMG (t=3.489, P=0.002). Meanwhile, MUP polyphasicity showed significant difference between MSA and non-MSA cases by EAS-EMG only (t=2.511, P=0.016). EAS-EMG showed more significant changes in neurogenic injury than US-EMG.

Conclusions: Both US-EMG and EAS-EMG are useful for the diagnosis of MSA. The differences of multiple indexes of EAS-EMG were more significant than those of US-EMG for MSA cases. US-EMG could be a supplement of EAS-EMG in case of restriction.

Keywords: External anal sphinter; Urethral sphincter; Electromyography; Multiple system atrophy

Introduction

Multiple system atrophy (MSA) is a sporadic and chronic degenerative movement disorder that is characterised by combination of autonomic failure, cerebellar ataxia, and Parkinsonism at various levels. It is still poorly understood. Because of various clinical manifestations, early diagnosis and differential diagnosis from other parkinsonism as well as Parkinson’s disease (PD) are difficult [1]. The distinction of MSA from PD is based on a well characterized clinical picture and on pathological identification of cytoplasmic inclusion bodies [2]. An accurate differential diagnosis between PD and MSA is extremely relevant for its prognostic and therapeutic implications but discrimination of the two diseases is often times challenging due to their broad clinical overlap [3].

External anal sphincter electromyography (EAS-EMG) is an established method to detect neurogenic change in motor unit potentials (MUP), which mostly reflects denervation and reinnervation of the sphincter muscle. The significance of EAS-EMG in MSA is well known [4]. EAS-EMG has been reported to be of value in the diagnosis of multiple system atrophy (MSA) because the degeneration of Onuf’s nucleus is a pathological hallmark of MSA [5-7]. However, the criteria for the detection of neurogenic changes in EAS-EMG differ among neurophysiology laboratories and this poses as a problem for neurologists in distinguishing MSA from other parkinsonian syndromes [8]. Although there are some limitations in evaluating the data sets gathered from EAS-EMG studies, for example, lack of age-matched normal control data, study showed that the mean duration of MUPs in EAS-EMG is the most appropriate parameter in differentiating MSA from other parkinsonian syndromes; however, EAS-EMG should be used as a supportive diagnostic tool for the diagnosis of MSA [8]. There are also negative reports of the diagnostic value of EAS-EMG [9].

The recording of urethral sphincter electromyography (US-EMG) has several clinical and experimental uses. In particular, with the development of animal models of stress urinary incontinence, the recording of US EMG has been vital to the study of the response of the US in maintaining urinary continence [10-14]. In recent studies, utilization of US EMG as a supplement to the external anal sphincter EMG (EAS-EMG) was proposed for routine electrophysiological method in patients with a suspicion of MSA [15-16]. The differences of
multiple parameters of EAS-EMG were more significant than those of US-EMG for MSA cases.

Compared with EAS-EMG, the diagnostic roles of US-EMG in MSA were rarely reported. To evaluate the diagnostic value of EAS-EMG and US-EMG in MSA, prospective observation was applied to MSA and non-MSA patients in this study.

Materials and Methods

Subjects

Patients from Department of Neurology, the Navy General Hospital participated in this study. Recruitment was lasted from June 2010 to October 2013. All patients were interviewed and examined by board-certified neurologists. Patients with a clinical diagnosis of MSA qualified with second consensus statement on the diagnosis of MSA by Gilman in 2008 were enrolled in the present studies [17]. Thirty-five (18 men, 17 women) patients with median age of 58.37±8.95 (range 44 to 76) underwent EAS-EMG and US-EMG. The course was between 0.5 and 7.7 (mean 3.6±1.7) years. Fifty-three (38 men, 15 women) non-MSA cases including 16 Parkinson’s Disease, 7 hereditary cerebellar ataxia, 7 cerebrovascular disease, 6 progressive supranuclear palsy, 5 multisystem lesions, 5 neurogenic bladder, 5 dystonia, 1 conus medullaris injury, 1 demyelination and 1 diabetes. There was disorder of urination and defecation with various degrees in all the cases. Median age was 60.61±12.5 (range 37 to 83) years. There was no significant difference of the age (t =0.973, p=0.333) and gender (x² =3.743, P=0.053) composition between the two groups (Supplemental file).

EAS-EMG and US-EMG

Keypoint type Electrical/trigger potentiometer of Dandi company was used with standard settings (filters, 20Hz- 10kHz). The sensitivity of mild contraction was 100uV/D with scanning speed 5ms/D, while that of strong contraction was 0.5V/D with scanning speed 200ms/D (PMID:17605352). EAS-EMG and US-EMG were carried out under the same condition for MSA and non-MSA patients. The studies were approved by ethics committees of our hospital.

EAS-EMG: Investigations were performed with the patients in the left lateral position with knees and hips flexed. Hips were aparted and at the back of left outside anus (about 4:30)10 mm the inner side of mucocutaneous junction, a concentric needle electrode was inserted into shallow strata of subcortex in external anal sphincter [5]. Electric activity of anal sphincter while relaxed (mimic defecation) as well as with mild and strong contraction (mimic discontinuous defecation) was recorded.

US-EMG: Investigations were performed with the patients in the horizontal position. A concentric needle electrode with 50mm long and diameter of 0.45mm was inserted into the middle of anus-bulbospongiosus for male patients. A concentric needle electrode with 75mm long and diameter of 0.65mm was inserted into 5mm besides external urethral orifice for female patients [18]. Sensation of resistance and myoelectricity are the signs of inserting into urethral sphincter. Electric activities of urethral sphincter in keeping urine phase and urinating phase was recorded.

Statistical analysis

SPSS17.0 was used for statistical analysis. Age, parameters of mean MUP duration and amplitude, percentage of polyphasic MUP, as well as amplitude when strong contraction of EAS-EMG and US-EMG were recorded and analyzed. Kollomogorov-Smirnoff one sample test was used to do the normality test. Among them, measurement data was in normal distribution, whose central tendency was expressed as ±s. Two independent t test is used to compare the two groups. For measurement data that is not in normal distribution, median and interquartile range were used to express central tendency and dispersion separately. Mann-Whitney U test, a non-parametric test was used to compare the two groups. Paired-sample T test and paired-Samplest test were used to compare parameters of EAS-EMG and US-EMG in MSA group. Pearson chi-square test was used to compare the difference of sex constituent ratio between MSA and non MSA group. Likelihood ratio chi-square was used to compare recruited pattern when strong contraction between the two groups. P<0.05 was regarded significant.

Results

Neurogenic injuries of MSA group showed in both US-EMG and EAS-EMG

Neurogenic injury was showed in US-EMG and EAS-EMG in 27 cases of MSA group (77.1%). The results of two methods were in compliance with each other. The injuries included prolonged mean MUP duration, increased amplitude and percentage of polyphasic MUP, as well as recruited pattern and amplitude when strong contraction showed simple phase or simple-mix phase with satellite potential. Similar pattern was observed in US-EMG and EAS-EMG in non-MSA group. Neurogenic injury was showed in 5 non-MSA cases, including 2 hereditary cerebellar ataxia, 1 Progressive supranuclear palsy, 1 neurogenic bladder and 1 diabetes(Figure 1 A and B).

EAS-EMG results between MSA and non-MSA groups

Thirty-four MSA patients underwent EAS-EMG (1 was not available because of perianal abscess). Forty-eight non-MSA patients underwent EAS-EMG (5 was not available because of haemorrhoids and anal fissure). MUP duration (ms) of MSA patients was 13.00±4.01 while that of non-MSA patients was 10.40±1.90 (t=3.515, P=0.001). Light contraction amplitude (uv) of MSA patients was 534.59±187.22
while that of non-MSA patients was 497.93±193.59 (t=0.856, P=0.395). Percentage of polyphasic MUP (%) of MSA patients was 40.07±24.36 while that of non-MSA patients was 249.00(210.00-340.00) (Z=5.281, P=0.000).

Comparison of recruited pattern when strong contraction between MSA and non-MSA groups

Within 34 MSA patients underwent EAS-EMG, 7 showed simple phase, 4 showed interference phase, 19 showed mix phase, while 4 showed simple-mix phase for amplitude when strong contraction; within 48 non-MSA patients underwent EAS-EMG, 6 showed simple phase, 9 showed interference phase, 32 showed mix phase, while 1 showed simple-mix phase for amplitude when strong contraction (Likelihood ratio was 4.927, P=0.177). Within 31 MSA patients underwent US-EMG, 7 showed simple phase, 2 showed interference phase, 18 showed mix phase, while 4 showed simple-mix phase for amplitude when strong contraction; within 52 non-MSA patients underwent US-EMG, 7 showed simple phase, 1 showed interference phase, 42 showed mix phase, while 2 showed simple-mix phase for amplitude when strong contraction (Likelihood ratio was 5.522, P=0.137). There was no significant difference of mean MUP amplitude for light contraction or strong contraction between the two groups. US-EMG mainly showed prolonged mean MUP duration in MSA group (Table 3).

Table 2: US-EMG results between MSA and non-MSA groups.

<table>
<thead>
<tr>
<th>No.</th>
<th>MUP duration (ms)</th>
<th>Light contraction amplitude (uv)</th>
<th>Percentage of polyphasic MUP (%)</th>
<th>Strong contraction amplitude (uv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSA</td>
<td>34</td>
<td>13.00±4.01</td>
<td>534.59±187.22</td>
<td>40.07±24.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.21±0.71</td>
<td>23.02±19.29</td>
</tr>
<tr>
<td>Non-MSA</td>
<td>48</td>
<td>10.40±1.90</td>
<td>497.93±193.59</td>
<td>27.98±13.57</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td></td>
<td></td>
<td>1.18±0.56</td>
</tr>
<tr>
<td>P value</td>
<td>0.001*</td>
<td>0.395</td>
<td>0.016*</td>
<td>0.897</td>
</tr>
</tbody>
</table>

Table 1: EAS-EMG results between MSA and non-MSA groups.

* P<0.05 Data was standard normal distribution. T test was used for analysis.

US-EMG results between MSA and non-MSA groups

Thirty-one MSA patients underwent US-EMG (1 refused, 3 were not coordinate). Fifty-two non-MSA patients underwent US-EMG (1 was not coordinate). MUP duration (ms) of non-MSA patients was 12.79±3.21 while that of non-MSA patients was 10.01±1.15 (t=6.896, P=0.000). Light contraction amplitude (uv) of MSA patients was 534.59±187.22 while that of non-MSA patients was 497.93±193.59 (t=0.856, P=0.395). EAS-EMG of MSA group showed prolonged mean MUP duration, increased percentage of polyphasic MUP compared with those of non MSA group (Table 1).

Comparison of indexes obtained in EAS-EMG and US-EMG of MSA group

Thirty-four MSA patients underwent EAS-EMG while 31 MSA patients underwent US-EMG. MUP duration (ms) in EAS-EMG was 13.00±4.01 while in US-EMG was 12.79±3.21 (Z=1.926, P=0.054). Light contraction amplitude (uv) in EAS-EMG was 534.59±187.22 while in US-EMG was 249.00(210.00-340.00) (Z=5.281, P=0.000). Percentage of polyphasic MUP (%) in EAS-EMG was 40.07±24.36 while in US-EMG was 23.02±19.29 (statistics=4.484, P=0.000). Strong contraction amplitude (uv) in EAS-EMG was 1.00 (0.80-1.35) while in US-EMG was 0.6 (0.50-1.15) (Z=6.896, P=0.000). In MSA group, EAS-EMG showed more significant changes in light contraction, percentage of polyphasic MUPs and mean MUP amplitude when strong contraction than US-EMG. There was no statistical difference in other indexes (Table 4).

Table 3: Comparison of recruited pattern when strong contraction between MSA and non-MSA groups.

<table>
<thead>
<tr>
<th>No.</th>
<th>MUP duration (ms)</th>
<th>Light contraction amplitude (uv)</th>
<th>Percentage of polyphasic MUP (%)</th>
<th>Strong contraction amplitude (uv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSA</td>
<td>31</td>
<td>12.79±3.21</td>
<td>249.00(210.00-340.00)</td>
<td>23.02±19.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.6 (0.50-1.15)</td>
<td>787.000</td>
</tr>
<tr>
<td>Non-MSA</td>
<td>52</td>
<td>10.01±1.41</td>
<td>304.5(230.25-418.00)</td>
<td>17.19±9.09</td>
</tr>
<tr>
<td>statistic</td>
<td>4.573</td>
<td>664.5</td>
<td>2.125</td>
<td>787.000</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>0.183</td>
<td>0.232</td>
<td>0.517</td>
</tr>
</tbody>
</table>

Table 2: US-EMG results between MSA and non-MSA groups.
US-EMG results between MSA and PD groups

Sixteen PD patients underwent US-EMG. MUP duration (ms) of PD patients was 10.32±1.21 (t=3.565, P<0.001). Light contraction amplitude (uv) of PD patients was 533.88±286.54 (t=0.011, P=0.992). Percentage of polyphasic MUP (%) of PD patients was 9.90±1.01 (t=4.593, P<0.001). Light contraction amplitude (uv) of PD patients was 276.00(238.25-424.00) (U=0.210, Z=4.484, P=0.000). Strong contraction amplitude (uv) of PD patients was 10.32±1.21 (t=3.565, P=0.001). Light contraction amplitude (mv) of polyphasic MUP (%) of PD patients was 1.32±0.44 (t=0.580, P=0.564). EAS-EMG of MSA group showed prolonged mean MUP duration, increased percentage of polyphasic MUP compared with those of non MSA group (Table 5).

Discussion

Autonomic nervous dysfunction such as disorders of urination and defecation is the main clinical manifestation and key diagnostic criteria of MSA17. Iwata evaluated sparing of the Onufrowicz nucleus in sacral anterior horn lesions and showed that Onufrowicz nucleus may be innervating the external sphincter muscle of the urethra and bladder. The results of our study support this hypothesis, as the percentage of polyphasic MUP was significantly higher in the MSA group compared to the PD group. This suggests that the external anal sphincter muscle may have a different autonomic innervation in patients with MSA compared to those with PD. However, further research is needed to confirm this hypothesis and to better understand the mechanisms underlying these differences.
the anus [19]. In patients with MSA the mechanism is a focal loss of motor neurons in Onuf’s nucleus [20,21].

The lost of neurons can be recorded by EAS-EMG and US-EMG, which makes early diagnosis possible [15]. Neurogenic injury was showed in EMG including prolonged mean MUP duration, increased percentage of polyphasic MUP as well as with spontaneous activity or satellite potential.

Clinically, autonomic nervous dysfunction includes orthostatic hypotension, abnormal sweating, disorder of urination and defecation, et al. Disorder of urination and defecation has various clinical manifestations. Some patients have frequent urination and uroeschisis, but do not have digestive manifestations such as constipation. Other patients have symptoms such as constipation and diarrhea, but do not have urethral symptoms. The correspondence between clinical manifestation and different EMG tests was evaluated. The results showed the same correspondence between clinical manifestation and the two EMG tests, which was the same as reports aboard [22-24]. Positive results of EMG can be observed even without clinical manifestations.

There was significant difference of light contraction, percentage of polyphasic MUP, as well as amplitude when strong contraction between EAS-EMG and US-EMG, especially that of percentage of polyphasic MUP. Because of the specific anatomic location of urethral sphincter, it is difficult to obtain data during US-EMG. Our previous studies showed that amplitude when light contraction has more diagnostic value in US-EMG than EAS-EMG for MSA15. However, it was not available in this large sample study.

Patients of neurogenic bladder, diabetes, progressive supranuclear palsy and hereditary cerebellar ataxia can have clinical manifestation of autonomic nervous system injury including dysfunction of bladder and rectum [25-27]. Neurogenic injury was showed in EAS-EMG and US-EMG of non MSA group, including 1 progressive supranuclear palsy, 1 neurogenic bladder, 1 diabetes and 2 hereditary cerebellar ataxia. Prolonged mean MUP duration was mainly showed in EMG. Our previous studies showed that amplitude when light contraction has more diagnostic value in US-EMG than EAS-EMG for MSA15. However, it was not available in this large sample study.

The diagnosis of MSA is mainly depended on clinical manifestations and nonspecific manifestations on brain image. Imaging tests show atrophy in the cerebral cortex, cerebella and brainstem in some patients. Generally, electrophysiological abnormalities occurred earlier than those of image. Neurogenic injury was showed in EAS-EMG and US-EMG as soon as symptoms of the autonomic nervous system emerged. The diagnosis of MSA using EAS-EMG was already carried out in a few hospitals in China with high positive rate and the comparison between EAS-EMG and US-EMG in MSA was reported recently [15]. It was also reported aboard that both EAS-EMG and US-EMG can record a focal loss of motor neurons in Onuf’s nucleus [28], which was consistent with our results.

Other assessments currently used for differential diagnosis of PD and MSA, such as composite autonomic severity score (CASS) [29] and metabolodobenzylguanidine myocardial scintigraphy [30], Ambulatory BP monitoring (ABPM), were also showed to offer good diagnostic accuracy. Nevertheless many of the tests required to obtain CASS can be performed only in specialized laboratories. Although ABPM is broadly available and relatively inexpensive and could be considered as a first step diagnostic tool to support clinical criteria before proceeding to more complex and costly procedures, it deserves further investigation.

Above all, there was certain value in US-EMG and EAS-EMG for the diagnosis and differential diagnosis of MSA. They could be used as routine electrophysiological methods for the patients who were suspected of MSA. They could be a supplement of each other in the case of contraindications including anal fistula, perianal and perineal abscess, et al. However, there are several limitations of this study. Our previous studies showed that amplitude when light contraction had more diagnostic value in US-EMG than EAS-EMG for MSA. However, there were only nine cases at that time and it was not available in this large sample study, that’s why the results are different. It showed that the result was significantly influenced by the number of cases. More cases are needed in future studies for further evaluation.

References


