External Anal- and Urethral-Sphincter Electromyography for Differentiating MSA-P, PD and PSP: Using a Needle to Sort the Haystack!

The Parkinson Plus syndromes (PPS), often referred to as atypical parkinsonism, comprise a diverse group of neurodegenerative disorders that are distinct from Idiopathic Parkinson's disease (IPD) in terms of their clinico-radiological features, levodopa non-responsiveness and rapid functional deterioration.[1] PPS disorders include progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD) and dementia with Lewy bodies (DLB). Although certain red flags including vertical supranuclear gaze palsy, frequent falls, overt dysautonomia, pyramidal tract signs, ataxia, apraxia, early onset dementia or hallucinations may help differentiate PPS from IPD, at times they closely mimic IPD especially in the early course of the disease process.[2]

In movement disorders clinics, about 80–85% of Parkinsonism patients exhibit the classic symptoms of IPD, the remaining 15–25% of patients come under the other group of neurodegenerative disorders including PPS.[3] PPS are uncommon disorders, with PSP being the most prevalent amongst them.[1] Due to lack of a definite clinical or investigational marker, these disorders are often misdiagnosed, resulting in possible underreporting of their incidence and prevalence.[1] Differentiation between IPD and PPS, especially in early stages of illness can be quite challenging. During the past few decades, the evolving diagnostic criteria for different PPS have incorporated plethora of clinico-pathological phenotypes and radiological characteristics. Nonetheless, it has been highlighted that the accuracy of diagnosis primarily depends on serial clinical examination, as the disease advances.

Besides overlap of various associated symptoms, dysautonomia, in particular, is regarded as a core clinical entity of MSA, which is observed due to early neuronal degeneration in sacral onuf's nucleus. Electromyography (EMG) of the anal and urethral sphincters is a robust approach for demonstrating denervation and renervation changes suggestive of neuronal loss, and its application in the early identification of MSA has drawn significant interest since 1978.[4] During external anal sphincter (EAS)-EMG, the needle is inserted into the superficial subcutaneous part of EAS innervated by the onuf's nucleus. EAS-EMG abnormalities have been reported in more than 70% of MSA cases.[5,6] At least 20 different motor unit potentials (MUPs) with their duration including late satellite potentials,[7] percentage of polyphasic MUPs along with amplitude and recruitment during maximal contraction are recorded. Anal muscle retains a specific tone and fires at a lower rate even when relaxed, making spontaneous activity (SA) challenging to measure and understand. Schwarz *et al*.,[8] Fowler and Kirby[9] and Palace *et al*.[6] have emphasised the importance of abnormal SA, which may be identified as positive sharp waves, fibrillation potentials and complex repetitive discharges, in distinguishing MSA from PD. Several authors suggest prolongation of MUPs as the most useful parameter favouring MSA, with a maximal duration of 10 ms being used as the cut-off as observed in more than 80% of studied patients.[6,10-12] According to Qiu *et al*.,[13] when the average MUP length was prolonged by nearly >10 ms, the sensitivity and specificity of EAS-EMG were 75.8% and 83.0%, respectively, whereas US-EMG were 63.0% and 86.5%. Nevertheless, using both the EAS-EMG and US-EMG in tandem would increase sensitivity to 85%.

Previous studies demonstrated that advanced PD patients had MUP alterations comparable to MSA.[14,15] Moreover, EAS-EMG abnormalities in MSA may become more evident as the disease progresses, with Sakakibara reporting it in 52% patients in the first year of diagnosis and 83% MSA patients by fifth year of diagnosis.[16] Recently, Todisco *et al*.[17] has explored the prognostic significance of EAS- EMG alterations in MSA and its co-relation with prevalence of bowel/bladder symptoms and poor outcome. Many studies have found EAS-EMG easier and better tolerated by patients when compared to urethral sphincter (US)-EMG. Although uncommon, abnormal sphincter EMG has been reported in early stages of PSP patients as well.[6,16,18]

In this issue of the journal, Jia S, *et al*.[19] performed a single-center, prospective, observational study and analysed EAS-EMG and US-EMG findings amongst 26 MSA-P patients, 100 PD patients and 22 PSP patients. While average amplitude of MUPs in EAS-EMG were comparable in the three groups, a significant difference was observed in average duration of MUPs, percentage of polyphasic MUPs, amplitude during strong contraction and the ratio of simple phase and simple-mix phase during maximal contractions. The average duration of MUPs was significantly longer in MSA-P patients in comparison with PD and PSP (MSA-P vs PD vs PSP = 12 ms vs 9.8 ms vs 9.9 ms; $P < 0.001$), with a higher percentage of polyphasic MUPs (MSA-P vs PD vs PSP = 40.3% vs 31.6% vs 38.3%; $P < 0.001$), which was consistent with previous studies.[20,21] The ratio of simple phase and simple-mix phase of MSA-P and PSP was significantly higher than that of PD (MSA-P vs PD vs PSP = 38.5 vs 9 vs 36.36; $P < 0.001$), while the amplitude during strong contraction of MSA-P was significantly lower than that of PD (MSA-P vs PD vs PSP = 1 mV vs 1.5 mV vs 1.2 mV; $P = 0.005$). US-EMG was analysed separately for male and female patients. In US-EMG of male patients, the average duration of MUPs and the ratio

of simple phase and simple-mix phase of US-EMG differed significantly ($P < 0.05$) in the three groups, but significant difference was not observed in the amplitude of MUPs, percentage of polyphasic MUPs and amplitude during strong contraction. The average duration of MUPs in male MSA-P was significantly longer than that in male PD and PSP (MSA-P vs PD vs PSP = 12.9 ms vs 9.8 ms vs 10.4 ms; $P = 0.001$) and the ratio of simple phase and simple-mix phase in male MSA-P was significantly higher than that in male PD (MSA-P vs PD vs PSP = 57.1% vs 10.9% vs 14.3%; $P = <0.001$). The US-EMG findings in male PD and PSP patients were comparable. Because of only one female in PSP group, US-EMG findings of only MSA-P and PD female patients were compared. The average duration of MUPs in female MSA-P was significantly longer than that in female PD (11.5 ms vs 9.8 ms; $P = 0.001$); the ratio of simple phase and simple-mix phase in female MSA-P was significantly higher than that in female PD (60.0% vs 9.4%, $P < 0.001$). This study highlights the importance of EAS-EMG and US-EMG, particularly the average duration of MUPs, in differentiating MSA-P from PD and PSP. Although the authors did not discuss, variability of sphincter abnormalities between the "on" and "off" phases of levodopa response may be explored, especially in patients with IPD and those PPS patients demonstrating at least partial levodopa-responsiveness early in their disease course.

Despite being technically challenging for both examiner and patients, sphincter EMG can serve as a reliable and useful tool to differentiate MSA from other Parkinsonian syndromes, especially early in the disease course.

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