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Possibility of Combined Assessment of Biomarkers in Early Parkinson's Disease

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Abstarct: ***Aims & Objectives: There is much evidence that the Parkinson's disease neurodegenerative process begins many years before the onset of motor manifestations. The aim of this study was to investigate the changes in substantia nigra hyperechogenicity and sympathetic skin response in early PD patients. Materials & Methods: 12 patients were studied of which 9 men and 3 women with newly diagnosed with PD, with probable PD, and without clinical evidence of autonomic dysfunctions. The clinical status of patients was evaluated according to the modified scale of Hoehn and Yahr 5 degrees to the second, inclusive. More pronounced changes were seen in 1.5 and 2 on the used scale. Simultaneously, the study of these biomarkers could provide information on morphological and autonomous changes as an opportunity for early assessment of PD. Conclusions: We demonstrated for the first time the combination of biomarkers and methods that could provide information on morphological and autonomous changes for the earlier diagnosis of PD.***

Keyword: Early Parkinson's disease, Ultrasound, Substantia niga, Sympathetic skin response

1. Introduction

There is convincing evidence that the Parkinson's disease (PD) neurodegenerative process begins many years before the onset of motor manifestations by an estimated 3–6 years [14]. Most patients with PD describe autonomic symptoms at the time of diagnosis suggesting that these features may have potential sensitivity as clinical biomarkers of the premotor phase [7].

In the literature there is evidence that dysfunction of substantia nigra (SN) hyperechogenicity on transcranial sonography (TCS), sympathetic skin response (SSR) might be risk markers of PD [1, 2, 3, 4, 5, 8, 11, 12, 13] for diagnosis.

Transcranial sonography had a sensitivity of 88.2%, a specificity of 77.0%, a positive predictive value of 12.7% and a negative predictive value of 99.4% for subjects with clinically definite PD at baseline. Substantia nigra hyperechogenicity may represent a useful biomarker for PD not only in a hospital-based setting but also in the general community [8]. In early PD patients, sympathetic skin response to demonstrate and to monitor the sympathetic cholinergic dysfunction, despite the lack of autonomic symptoms [5].

The aim of this study was to investigate the changes in substantia nigra hyperechogenicity and sympathetic skin response in early PD patients.

2. Materials and Methods

Twelve patients were studied of which 9 men (75%) and 3 women (25%) newly diagnosed with PD, with probable PD, and without clinical evidence of autonomic dysfunctions. Patients were not taking antidepressants. The clinical status of patients was assessed according to the modified scale of Hoehn and Yahr in 5 stages [6].

Transcranial sonography of SN was performed in supine position with the head slightly elevated. Used Philips iU 22 ultrasound with phase array whit a frequency of 1-5 Mhz. The survey was conducted on a standardized methodology. The butterfly shaped mesencephalic area (of low echogenicity) and surroun ding hyperechogenic basal cisterns were examined in the axial plane paralleling the orbitomeatal line According to international data 4,6, extreme superior values (i.e. values above 0.5 cm) were considered outliers and excluded phased-array transducer, penetration depth of 14.0-16.0 cm, dynamic range of 45-55 dB, and moderate suppresion of low echo signals [2, 11].

Level assessment of echogenicity of substantia nigra was evaluated by the scale of Bártová et al. P [2]. Sympathetic skin response is recorded on standard EMG equipment. The active silver/silver electrodes are placed in the palm or sole with the reference over the dorsum of the respective body part, after cleaning the skin surfaces and using electrolyte gels [6, 12].

Scale with lowered amplitude was used and decreased latency (mild; expressed) against healthy side like self-control and according to the known reference values in the literature [5, 10, 12].

3. Results

In one patient (8.33%) did not conduct the study due to lack of temporal window. SSR was conducted on 11 patients. Patients with early PD used in clinical modified rating scale of Hoehn and Yahr have second degree (included) - 12 (100%). 6 of these -1 degree (50%) 5 -1.5 degree (33.3%), 1- second grade (16.6%). The drop out patient was with grade 2 from the used scale.

Table 1: *Results transcranial sonography, sympathetic skin response - tests and Modified Hoehn and Yahr Scale*

Echogenicity Same as brain stem - 2 (18.18%)	Very low but clearly detectable area of SN - 4 (36.36%)	Medium, lower than perimesencephalic cisterns – 4 (36.36%),	Same as perimesencephalic cisterns- 1 (9.09%)	Higher than perimesencephalic cisterns -0
SSR (latency, amplitude) normal – 1 (9.09%)	Low amplitude – mild degree;4 (36.36%) Ipslilateral	Low amplitude – pronounced; 5 (45.45%) ipsilatreal-	Low amplitude and latency pronounced; 1 (9.09%) Ipsilateral	0
Modified Hoehn and Yahr Scale	1 – 6 (50%)	1.5 – 4 (33.3%)	2-1 (9.09%%)	0

4. Discussion

Identification of risk factors and prodromal markers for Parkinson's disease and the understanding of the point in time of first occurrence is essential for the early detection of incident PD [7].

Studied patients by us had second degree by the Modified Hoehn and Yahr Scale. Males were prevalent (75%). Found changes in transcranial sonography show first level on the scale in 6 patients (50%) changes in TCS-very low but clearly detectable area of SN, but in 4 patients (36.36%) changes in SSR are with mild lowered amplitude ipsislateral. At 1.5 on a scale of SN TCS changes show - medium, lower than perimesencephalic cisterns in 4 (36.36%) and SSR pronounced decrease in amplitude at 5 (45.45%) ipsilateral. In grade 2 scale has only 1 patient with changes in TSC- same as perimesencephalic cisterns in one patient 1 (9.09%), and changes in SSR are expressed with lowered amplitude and reduced latency.

In 37 month longitudinal study of 1847 patients in 3 centers was demonstrated for the first time a highly increased risk for PD in elderly individuals with SN+Transcranial sonography of the midbrain may therefore be a promising primary screening procedure to define a risk population for imminent PD [4]. The SN area was also dependent on the stage [2].

In patients with advanced PD is demonstrated a significant difference between the earliest and the most advanced PD stage and control groups in terms of changed sympathetic skin response [13].

Based on literature data sympathetic skin response can help in the differential diagnosis of PD [1].

Independently from the peripheral or central origins of such phenomena, these findings suggest that simultaneous bilateral SSR amplitude evaluation could be useful, in early IPD patients, to demonstrate and to monitor the sympathetic cholinergic dysfunction, despite the lack of autonomic symptoms [5].

5. Conclusions

In the proposed pilot study we demonstrated for the first time the combination of biomarkers and methods that could provide information on morphological and autonomous changes for the earlier diagnosis of PD.

The authors declare no conflict of interests.

Acknowledgments

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