Multimodal Evoked Potentials in Primary Sjögren's Syndrome Without Neurological Manifestations

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Summary

We evaluated multimodal evoked potentials in patients with primary Sjögren's syndrome without clinical neurological manifestations. While brainstem auditory evoked potentials (BAEP) were performed in ninety patients visual (VEP) and somatosensory evoked potentials (SEP) could be evaluated in fifty-eight patients. The control group included 20 healthy adults matched for sex and chronological age. VEP and BAEP studies did not reveal any abnormality. In SEP; N9-N13 interpeak latencies were significantly prolonged in the patients group. However, the latency of N9 potentials recorded from Erb's point was normal as well as the N13-N20 interpeak latencies. This result indicates that central branches of the primary sensory neurons are involved in Sjögren's syndrome.

Key words: Primary Sjögren's syndrome, VEP, BAEP, SEP

INTRODUCTION

Primary Sjögren's syndrome (PSS) is a chronic inflammatory autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, resulting in dry eyes and dry mouth. Apart from sicca symptoms due to the glandular affection various extraglandular manifestations may develop, including central and peripheral nervous system. PSS may affect the entire neuraxis, including the brain, brain stem, spinal cord, optic nerves and peripheral nerves. The neurological abnormalities may be subtle, usually of insidious onset, less often they may have an acute or subacute onset. In the course of the disease neurological deficits are characteristically transient and usually resolve with time. However, central nervous system (CNS) involvement may have a chronic and...
progressive course and is devastating. Therefore, detecting the subclinical abnormalities in CNS-PSS is important. This approach may be useful in the diagnosis and follow-up of the CNS involvement.

Multimodal evoked potentials (MMEP) including visual (VEP), brainstem auditory (BAEP), somatosensory evoked potentials (SEP) can be used in the evaluation and follow-up of patients with CNS-PSS. Apart from this, MMEP study may detect subclinical abnormalities in CNS-PSS. The aim of the present study was to assess the utility of evoked potentials in patients with PSS without clinical manifestations of central or peripheral nervous system involvement.

MATERIAL AND METHODS

Ninety consecutive patients (10 male, 80 female, aged 18-68 years, mean: 47.6 years) with PSS referred from the Rheumatology Department were evaluated. All the patients fulfilled the American-European Consensus Group criteria. Evaluation included a detailed neurological history, examination and multimodal evoked potential studies (VEP, BAEP, SEP). While BAEPs were evaluated in all the patients, VEP and SEP could be performed in fifty-eight patients because of technical causes. Nihon Kohden Neuropack 8 4200 K was used for the recordings and the recordings electrodes were Ag/AgCl surface electrodes.

The control group included 20 healthy adults matched for sex, chronological age and height.

Pattern-reversal VEPs (PVEPs) were obtained by using a black-and-white checker board displayed on a television screen which reversed each second. Each check subtended 37° of visual field. Recordings were performed in a dark room after monocular full-field stimulation with the active scalp electrode being Oz, referenced to Cz. The ground electrode was placed around the forearm. An examiner watched the patients and the normal controls during VEP recordings to sustain their fixation on the television screen. The frequency limits were set at 2-100 Hz and the analysis time was 500 ms. A total of 256 responses were averaged. The latency and the peak amplitude values of the P100 components were taken into consideration.

For BAEPs ipsilateral mastoid-Cz electrodes were used for recordings. Following amplification (bandpass 100Hz-3kHz) 1024 individual responses were averaged with an analysis time of 10ms.10 Hz clicks at 90 dBAHL were given and the contralateral ear was masked with 40 dBHL noise. Absolute latency of wave I, I-III, III-V interpeak latencies (IPL) were taken into consideration.

The SEPs were recorded bilaterally by stimulating the median nerve at the level of wrist by using a bipolar surface electrode. Recordings were made from (2 cm posterior to C3, C4 of the international’ and C4’the contralateral C3 10-20 system ), the posterior neck at the level of C2, and the Erb's point with Ag/AgCl surface electrodes. A common reference electrode was placed on Fz. The stimulus frequency was 2 Hz. The frequency limits were set at 20 Hz- 3 KHz. 256 responses was averaged. The latency and the peak amplitude values of N20 and the latencies of N9 and N13 were selected for evaluation.

Informed consent was obtained from all the patients.

Student-t test was used for the comparison of means. Significance was assumed at p< 0.05.

RESULTS

A total of the ninety patients with PSS were evaluated. None of the patients complained about neurological symptoms. No neurological abnormalities could be detected on examination.
VEP study was performed on fifty-eight patients. When the amplitude and the latency values of P100 recorded in patients were compared with the normal controls a statistically significant difference could not be found.

BAEP recordings were made in ninety patients. When compared with the results of the normal controls absolute latency of the first component, I-III and III-V IPL were not significantly different in the patient group.

SEPs were recorded by median nerve stimulation in fifty-eight patients. The mean latency values of N9 potentials recorded from the Erb's point were not statistically different from the normal controls (p=0.148). Absolute latencies of N13 (p=0.001) and N20 potentials (p=0.017) were prolonged (Table 1). These results were due to prolongation of the N9-N13 IPL (p= 0.001) (Figure 1). Patients and controls with pathological SEP latencies were given table 2. However N13-N20 IPL was not significantly different from the normal controls (p=0.79).

| Table 1: SEP latency values in patients group and controls and the statistical results. |
|---------------------------------|-------|-------|-------|-------|-------|-------|
| Latency (ms)                   | (ms)  | (ms)  | (ms)  | (ms)  | (ms)  | (ms)  |
| Patients Mean                  | 19.66 | 8.62  | 14.64 | 11.03 | 5.01  | 6.022 |
| SD                             | 1.35  | 0.52  | 0.77  | 0.92  | 0.88  | 0.47  |
| Controls Mean                  | 18.82 | 8.43  | 13.41 | 10.39 | 5.41  | 4.98  |
| SD                             | 1.15  | 0.45  | 0.39  | 0.74  | 0.82  | 0.12  |
| Significance                   | P= 0.017 | P= 0.148 | P< 0.001 | P= 0.06 | P= 0.79 | P< 0.001 |
| Observed power                 | 0,677 | 0,303 | 1,000 | 0,794 | 0,421 | 1,000 |

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<th>Table 2: Patients and controls with pathological SEP latencies</th>
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<td>N20 (ms)</td>
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DISCUSSION

PSS diagnosis was established in our patients according to American-European Consensus Group classification criteria of Sjögren's syndrome which provides high sensitivity and specificity. The true incidence and prevalence of neurological manifestations in PSS vary in various series reported in the literature. The neurological manifestations must be recognized early so as to avoid long term complications that would reduce the probability of success with treatment.

Peripheral neuropathy is the most common neurological complication of PSS affecting clinically as many as 21.7% of patients. 50% of patients have subclinical neuropathy revealed by a systematic electrophysiological study.

CNS complications have been described in up to 50% of the patients depending upon the population studied. It is still a matter of debate whether CNS involvement is due to generalized vasculitis or an organ-specific antibody reaction. Diagnosis of CNS-PSS requires a high index of suspicion and specialized clinical testing. In PSS, focal and diffuse CNS disease may mimic multiple sclerosis (MS). MM EP results in CNS-PSS are often indistinguishable from those observed in MS. Approximately 50% of patients with clinical CNS-PSS have one or more abnormal MMEP tests. As in MS, functional abnormalities delineated by MMEP testing often establish the presence of subclinical disease in CNS-PSS.

Our study was planned to determine if MMEP abnormalities could help us to detect subclinical neurophysiological dysfunction in those with PSS. In a previous study, high frequency (12% of 48 PSS patients) of abnormalities on VEP testing has been reported in asymptomatic PSS, suggesting subclinical involvement. In another study of 20 patients with PSS, pathological tibial SEP was seen in only one patient without neurological involvement. BAEPs were normal in the same study. These studies included a few number of patients. Alexander et al. stated that they had not performed similar neurodiagnostic testing on asymptomatic patients in their institution.
In our study VEP and BAEP studies no abnormality was present. In SEP studies, the latency of N9 potentials recorded from Erb's point was normal. However absolute latency of N13 and N20 potentials were prolonged due to prolongation of the N9-N13 IPL, when compared with the normal controls.

Our patients had no symptoms or signs indicating a peripheral neuropathy and peripheral nerve conduction studies were not performed. Despite a normal latency N9, prolongations of N9-N13 IPL indicate that peripheral branches of the primary sensory neurons were not involved whereas the central branches were. It has been suggested that the dorsal root ganglia are pathologically and primarily involved with T cell invasion in Sjögren cases. (7,9,13) Our results are consistent with this pathological view of ganglioneuropathy. Apart from this, the delayed latencies in SEP may be related to impaired neuronal activity due to small blood vessel vasculitis on the pathway from Erb's point to C2 spinal level.

The aim of our study was to find out subclinical CNS involvement in patients with PSS and peripheral nerve conduction studies were not a part of this study. As indicated above VEP, BAEP or SEP changes showing a central involvement could not be detected. The predominating abnormality was the prolongation of the N9-N13 IPL which is in favour of a central axonopathy and/or dorsal root ganglioneuropathy.

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REFERENCES


