Somatosensory Evoked Potential Findings in Ankylosing Spondylitis

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Abstract

Objective: Somatosensory evoked potential (SSEP) abnormalities were reported in patients with ankylosing spondylitis (AS). This study aimed to investigate SSEP abnormalities and its relation with clinical findings in AS patients.

Materials and Methods: The study included 26 patients with AS and 17 age-matched health volunteers (Control for SSEP). Median nerve SSEP findings were normal in all AS cases. However, delayed latency and/or very low amplitude of tibial nerve SSEP was found in 20 (76.9%) AS patients. There were significant correlations between tibial SSEP latency and disease duration (R=0.433 to 0.635). There was also an inverse correlation between tibial SSEP amplitude and disease duration (R=-0.429, p=0.047). Serum estradiol level, hip total bone mineral density, The Bath Ankylosing Spondylitis Functional Index (BASFI) score and Beck depression score were significantly lower in AS patients with SSEP abnormalities (37.3±10.8 pg/mL, 0.916±0.123 g/cm², 35.0±27.9, 12.8±8.4, respectively) than in AS patients without SSEP abnormalities (53.7±12.3 pg/mL, 1.103±0.197 g/cm², 64.8±15.5, 24.8±10.1, respectively).

Conclusion: Significant inverse correlations between SSEP latencies and dehydroepiandrosterone sulphate (DHEAS) levels were found (R=-0.400 to -0.713). There were also significant inverse correlation between SSEP latencies and DHEAS/oestrogen index (R=-0.596 to -0.868), and between SSEP latencies and DHEAS/Progesterone index (R=-0.467 to -0.685). As a conclusion, this study indicates that tibial nerve SSEP abnormalities are common in patients with AS and there are significant correlations between clinical findings of AS and SSEP abnormalities.

Key Words: Ankylosing spondylitis, clinical findings, neurologic involvement, somatosensory evoked potentials

Özet

Amaç: Somatosensoriyal uyandırılmış potansiyel (SUP) bozuklukları ankleozan spondilit (AS) hastalarda bildirilmektedir. Çalışmanın amacı AS hastalarında amacı SUP anormallikleri ve AS’nin klinik bulguları ile ilişkisini araştırmaktır.


Bulgular: Tibial SUP latansı ve hastalık süresi arasında anlamlı ilişki vardı (R=-0.433-0.635). Tibial SUP amplitüdü ve hastalık süresi arasında da ters bir ilişki vardı (R=-0.429, p=0.047). SUP anormalliği olan AS hastaları, SUP anormallığı olmayan AS hastalarına göre serum estradiol seviyesi, kalça toplam kemik mineral yoğunluğu, Bath Ankilozan Spondilit Fonksiyonel İndeks (BASFI) skoru ve Beck depresyon skoru (sarasyla 37.3 ± 10.8’ye karşı 53.7±12.3 pg/mL, 0.916±0.123’ye karşı 1,103±0.197 g/cm², 35,0±27.92’ye karşı 64,8±15,5 ve 12,8±8,4’e karşın 24,8±10,1) daha düşüktü.

Sonuç: SUP latansları ve dihidroepiandrosteron sulfat (DHEAS) seviyeleri arasında anlamlı ters ilişki bulundu (R=-0.400 - (-0.713)). SUP latansları ile DHEAS/oestrojen indeksi ve DHEAS/progesterone indeksi arasında anlamlı ters ilişki bulundu (sarasyla R=-0.596 - (-0.868) ve R= (-0.467) - (-0.685)). Sonuç olarak AS’li hastalarda tibial SUP bozuklukları siktir ve AS’nin klinik bulguları ile anlamlı ilişkilidir. AS’nin patogenez ve klinik bulguları üzerinde potansiyel nörolojik mekanizmaların etkisi araştırılmak daha fazlasaida daha iyi arastırılmak daha fazla sayıda hasta içeren yeniden araştırılmalıdır.

Anahtar Kelimeler: Ankilozan spondilit, klinik bulgular, nörolojik tutulum, somatosensoriyel, uyandırılmış potansiyel

Introduction

Ankylosing spondylitis (AS) is a well-known inflammatory chronic rheumatic disease primarily affecting the axial joints and seen more frequently in males under 40 years of age [1]. Though infrequent, neurological complications related with this disease have been reported in the literature. Nervous system involvement, more of the central nervous...
system (multiple sclerosis, cauda equina syndrome, focal epilepsy, vertebrobasilar insufficiency) and less of the peripheral nerves, is known in AS [2-4].

The fragility of the ankylosed spinal column and its susceptibility to fractures may well lead to atlanto-axial subluxation and spinal cord injury due to vertebral fractures and/or dislocations. Also there may be other late neurological complications such as arachnoid diverticuli within the lumbar column resulting in cauda equina syndrome [1-6]. Conversely, in some recent reports, an association with AS and multiple sclerosis (MS) has also been reported [1, 6-8]. A small number of studies recorded the variable results of electromyography in AS [2-4, 9, 10].

Somatosensory evoked potential monitoring is reproducible, reliable and frequently used to detect changes in electrophysiological conduction in peripheral nerves and central nerve pathways and therefore, to prevent nervous system damage. A significant change in the somatosensory evoked potential (SSEP) responses is indicated by a decrease in amplitude and/or an increase in latency. The abnormalities detected by SSEP do not provide a specific diagnosis but point to impaired function in that particular sensory pathway [11]. Pillay et al. [12] studied visual, brainstem auditory and somatosensory evoked potentials in 30 patients with AS. Abnormalities in somatosensorial evoked potential studies examining the visual pathways were recorded in 18 (60%) patients. Somatosensory evoked potentials were abnormal in 19 (63%) patients, and 9 patients (30%) had impaired function on brainstem auditory evoked potentials. Ramos-Remus et al. [13] also reported abnormal SSEP findings in only 14.6% of their patients with AS.

Neurological impairment in the course of AS is of paramount importance. In these conditions SSEP analyses may be critically important in the clinical setting. The results of studies evaluating the sensory pathways in patients with AS are confusing. The present study was designed to investigate any pathological finding in SEP studies and its possible relationship to clinical and laboratory results related with AS.

Materials and Methods

Study design

Forty-three voluntary males were included in the present study (26 AS, 17 healthy controls). The diagnosis of AS was made according to the modified New York criteria. The mean age of the sample was 41.5±8.9 years and the mean duration of disease of the patients was 11.6±7.3 years. Seventeen healthy males (age: 35.7±8.7 years, height: 176.6±6.4 cm) served as the control group. After detailed history and physical examination, all the patients were assessed by Bath Ankylosing Spondylitis Functional Index (BASFI) and depression by Beck Depression Inventory, which is a well-known instrument for measuring the severity of depression. All volunteers gave informed consent to the procedures.

Methods

Serum testosterone, dehydroepiandrosterenedione (DHEAS), estradiol, progesterone, follicle stimulating hormone and luteinizing hormone levels were also measured. From all the participants’ vertebral column and pelvis X-rays were taken.

SSEP studies both in AS and control groups were performed bilaterally from median and tibial nerves using Medelec Sapphire 4ME device. The stimulation duration was 200 micro seconds. The stimulus intensity was arranged to elucidate minimal movement in the first digit in the hand for median nerve and also for the first digit in the foot for tibial nerve. Stimulus frequency was 3 per seconds. For median SEP an active electrode was placed at the C3 for right median nerve and at C4 for left median nerve as channel 1 on Erb’s point, channel 2 on C5 and channel 3 in sculp, according to the international 10-20 system. Reference electrode for all 3 channels was chosen as Fz. For tibial SEP, an active electrode in channel 1 and its reference were placed on the popliteus and 3cm. proximally of the knee, respectively. Active electrode in the channel 2 and its reference was placed in the line of L4 on the midline and in the line of spina iliac anterior superior, respectively. At the channel 3, active and reference electrode were placed on Fz and Cz, respectively. Sensitivity was 50 microvolt; 10-2000 Hz.band-pass filters were used. 128 stimuli at median nerve stimulation and 512 stimuli at tibial nerve stimulation were averaged. Each record was done at least twice. The response for median SSEP from the Erb’s point, cervical and cortex were marked as N9, N13 and N20, respectively. The response for tibial SSEP from the popliteus and lumbar region were marked as N7 and N20, respectively. P1 was the first positive deflection that was recorded in the cortex and N1 was to the first negative deflection that was recorded in the cortex. P2 and N2 were named as the second deflections, respectively. Longer latencies than 3 standard deviation compared to the control group were considered as pathological. Amplitude lower than 50% compared to the control group was accepted pathological.

Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 16.0 for Windows. The arithmetic mean and standard deviation of the data were determined. Mann-Whitney U test was used to compare the average measurements and Spearman’s correlation test was applied for correlation analysis. If the correlation constant (R) >0.20 and p value of <0.05 were accepted to be statistical significant.
Results

Tibial SSEP latencies and/or amplitudes in 20 (76.9%) patients were not within the normal range. In 17 (65.4%) patients either prolonged latencies or low amplitude values were recorded. Conversely, in 3 (11.5%) patients had abnormality in both of these findings. Right and left median/tibial SSEP latencies did not show significant difference in average between the two groups (Table 1).

A statistically significant decrease was observed in tibial SSEP amplitudes compared to the control group (Table 2). Also we observed a positive correlation between SSEP latencies and disease duration and a negative correlation between SSEP latencies and disease duration (Table 3). Another important finding was the positive correlation between the disease activity and the increase in tibial SEP amplitudes (Table 4). In cases with pathological SSEP responses estradiol levels, BASFI and Beck Depression scores were found to be significantly lower when compared to those without any pathology (Table 5).

There was not any significant change observed at the duration of disease, chest expansion, finger-ground distance, age, height and other hormones. A significant negative correlation was determined between tibial SSEP latency and serum DHEAS level (Table 6) and a significant negative correlation was determined between the tibial SSEP latency and serum DHEAS/Estradiol and DHEAS/Progesterone level (Table 7).

Discussion

Our study continued with the hypothesis that some potential neurologic mechanisms have a role at the progression of AS. We observed that tibial SSEP amplitudes of AS patients lower compared to the control group. Therefore,
tibial SSEP pathology in AS patients might be associated with the clinical findings.

Increases in the erythrocyte sedimentation rate, CRP, trombocyte and IgA levels and a slight anemia occurs in the active period of AS disease [14]. In the active period of AS, serum estrogen and progesterone levels decrease but androgen and DHEAS levels increase [15]. In some studies an increase at androgen/estradiol ratio in AS patients is reported. The increase of DHEAS, estradiol and progesterone inhibition can be important in the pathogenesis of AS [16-18]. Hence the use of oral estrogen in women and the use of HCG (human chorionic gonadotropin) in men caused a significant decrease at the testosterone/estradiol ratio, erythrocyte sedimentation rate, IgA level, pain level, chest expansion, swelled peripheral joint number and also caused a significant recovery at the morning stiffness [14, 15, 19].

In this study, an increase is determined at the SSEP amplitude with leukocyte, platelet and IgA level. In the DHEAS level which an increase was reported, a shortening in tibial latency inversely proportional with DHEAS/estradiol ratio is determined. Serum estradiol level, functional capacity and depression score is determined lower at the patients who have SSEP pathology. We detect an increase at the latency and decreases at the amplitude, while the disease activity increased in this study.

Pathophysiology of SSEP abnormalities is unknown; also it was recommended that caution should be exercised in interpreting delayed evoked potentials if multiple sclerosis is suspected in a patient with AS [12, 13].

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Consequently, as our results, there is a tibial SSEP pathology in patients with AS and there is also an association between tibial SSEP pathology and the chronicity of the disease, sex hormones, functional status and depression in patients with AS. The results of this study show that there is a relation between the clinical findings and some potential neurologic mechanisms that can be effective on the pathogenesis and prognosis of the AS. Further studies are needed to determine the certain effect of potential neurologic mechanisms on the pathogenesis and clinical findings of AS.

Table 4. Correlation between tibial somatosensory evoked potential (SSEP) amplitude and disease activity

<table>
<thead>
<tr>
<th>Leukocyte</th>
<th>Trombosit</th>
<th>IgA</th>
<th>Right P1</th>
<th>0.453</th>
<th>0.039</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right N1</td>
<td>0.457</td>
<td>0.414</td>
<td>0.340</td>
<td>0.037</td>
<td>0.070</td>
</tr>
<tr>
<td>Right P2</td>
<td>0.362</td>
<td>-</td>
<td>-</td>
<td>0.098</td>
<td>-</td>
</tr>
<tr>
<td>Left P1</td>
<td>0.595</td>
<td>-</td>
<td>0.561</td>
<td>0.004</td>
<td>0.008</td>
</tr>
<tr>
<td>Left N1</td>
<td>0.499</td>
<td>-</td>
<td>-</td>
<td>0.021</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 5. Correlation between presence of tibial somatosensory evoked potential (SSEP) and BASFI, Beck depression scale scores and estradiol levels in the patients with ankylosing spondylitis

<table>
<thead>
<tr>
<th>Leukocyte</th>
<th>Trombosit</th>
<th>IgA</th>
<th>No (n=6)</th>
<th>53.7±12.3</th>
<th>64.8±15.5</th>
<th>24.8±10.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n=20)</td>
<td>37.3±10.8</td>
<td>35.0±27.9</td>
<td>12.8±8.4</td>
<td>0.029</td>
<td>0.021</td>
<td>0.030</td>
</tr>
</tbody>
</table>

Table 6. Correlation between tibial somatosensory evoked potential (SSEP) latency and serum DHEAS levels

<table>
<thead>
<tr>
<th>Leukocyte</th>
<th>Trombosit</th>
<th>IgA</th>
<th>DHEAS</th>
<th>-0.400</th>
<th>-0.480</th>
<th>-0.713</th>
<th>-0.581</th>
</tr>
</thead>
<tbody>
<tr>
<td>p</td>
<td>0.059</td>
<td>0.024</td>
<td>0.000</td>
<td>0.005</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Correlation between tibial somatosensory evoked potential (SSEP) latency and DHEAS/estradiol and DHEAS/progesterone

<table>
<thead>
<tr>
<th>Leukocyte</th>
<th>Trombosit</th>
<th>IgA</th>
<th>DHEAS/ Estradiol</th>
<th>DHEAS/ Progesterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right P1</td>
<td>-0.473</td>
<td>-</td>
<td>0.088</td>
<td>-</td>
</tr>
<tr>
<td>Right N1</td>
<td>-0.596</td>
<td>-0.467</td>
<td>0.025</td>
<td>0.044</td>
</tr>
<tr>
<td>Right P2</td>
<td>-0.727</td>
<td>-0.563</td>
<td>0.003</td>
<td>0.012</td>
</tr>
<tr>
<td>Right N2</td>
<td>-0.868</td>
<td>-0.551</td>
<td>0.000</td>
<td>0.014</td>
</tr>
<tr>
<td>Left P1</td>
<td>-0.806</td>
<td>-0.490</td>
<td>0.001</td>
<td>0.033</td>
</tr>
<tr>
<td>Left P2</td>
<td>-0.692</td>
<td>-0.461</td>
<td>0.009</td>
<td>0.047</td>
</tr>
<tr>
<td>Left N2</td>
<td>-0.687</td>
<td>-0.685</td>
<td>0.010</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SSEP: Somatosensory evoked potential; DHEAS: Dehydroepiandrosterone sulphate; BASFI: The Bath Ankylosing Spondylitis Functional Index
Conflict of Interest: No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this study.


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