Neurophysiologic Study in Patients With Rheumatoid Arthritis With Atlantoaxial Subluxation

Antonio Juan, a José Valverde, b Mónica Veciana, c and Jorge Montero c

Introduction: Radiological studies show that 80% of rheumatoid arthritis (RA) patients with more than 10 years present spinal afflictions and 40% of those patients will present neurological deterioration. The somatesthetic evoked potential (SEP) and the transcortical magnetic stimulation (TMS) are neurophysiologic studies that may be useful in early diagnosis of neurological damage.

Objective: To compare the results of the neurophysiologic studies (SEP and TMS) carried out on patients affected with RA without neurological clinic, with or without atlantoaxial subluxation (AAS), and in this way evaluate the efficacy of early diagnosis of the affection of the spinal medulla by electrodiagnostic methods.

Material and methods: Cases and controls study that included 29 patients affected with RA of more than 3 years evolution. All of the patients had 2 electrophysiological techniques carried out on them: SEP and TMS in the neurophysiologic laboratory.

Results: Twenty-nine patients participated in the study, of which 21 were females and 8 males. In the group affected with AAS 2 patients presented anomaly in the SEP (11.7%) and 7 in the TMS (41.1%). In the group without AAS 2 presented an altered TMS (16.6%), but no alteration in the SEP. No patient affected or not with AAS, presented alteration of both electrophysiological tests. No significant differences were found between the positivity of the RF or the presence of erosions and the affection of the atlantoaxial joint. No differences between the age of outset or years of evolution and the AAS.

Conclusions: In our study patients with AAS showed a greater trend towards the presence of alterations in the electrophysiological studies than the patients without AAS.

Key words: Rheumatoid arthritis. Cervical spine. Neurophysiologic studies.

Estudio neurofisiológico en pacientes con artritis reumatoide y subluxación atloaxoidea

Introducción: Los estudios radiológicos demuestran que el 80% de los pacientes afectos de artritis reumatoide con más de 10 años de evolución presentan afectación cervical y que el 40% de ellos presentaba deterioro neurológico. Los potenciales evocados somestéticos (PES) y la estimulación magnética transcortical (PEM) son estudios neurofisiológicos que pueden ser útiles para un diagnóstico precoz de daño neurológico.

Objetivo: Comparar los resultados de los estudios neurofisiológicos (PES y PEM) practicados a pacientes afectos de artritis reumatoide sin clínica neurológica, con y sin subluxación atloaxoidea (SAA), y valorar la eficacia del diagnóstico precoz de la afección de la médula espinal por métodos de electrodiagnóstico.

Material y métodos: Se trata de un estudio de casos y controles que ha incluido a 29 pacientes afectados de artritis reumatoide de más de 3 años de evolución. A todos los pacientes se les ha practicado 2 técnicas electofisiológicas: PES y PEM en el laboratorio de neurofisiología y se han separado los dos grupos según presentaran o no SAA.

Resultados: Participaron en el estudio 29 pacientes, 21 mujeres y 8 varones. En el grupo con SAA, 2 presentaron una anomalía en el PES (11,7%) y 7 en la PEM (41,1%). En el grupo sin SAA, 2 presentaron una PEM alterada (16,6%) pero ninguno en el PES. Ningún paciente, afecto o no de SAA, presentó alteración de ambas pruebas electrofisiológicas. No se encontraron diferencias significativas entre la positividad del factor reumatoide o la presencia de erosiones y la afectación de la articulación atloaxoidea. Tampoco se encontraron diferencias entre la edad de presentación o los años de evolución y la SAA.

Conclusiones: En nuestro estudio los pacientes con SAA mostraron una mayor tendencia a presentar alteraciones en los estudios neurofisiológicos que los pacientes sin SAA.

**Introduction**

The cervical column is commonly affected in rheumatoid arthritis (RA). The most common affection is atlantoaxial subluxation (AAS) that can present as 1 of several types: anterior subluxation, which is most frequent, vertical, lateral, and posterior. Prevalence of AAS varies from 19% to 70% of RA affected patients, and can present itself from the onset. It is related to disease activity and erosions in the peripheral joints and with a reduction in bone mass. Radiological studies demonstrate that 80% of patients with RA have cervical affection at 10 years and 40% of them will have a neurological deficit. Clinical manifestations of AAS are cervical pain, rigidity, reduction in mobility as well as motor, and sensitive deficits that can be caused both by mechanical compression of the spinal cord and by vascular alterations. Mortality increases in patients with RA and cervical column affection, though this is rarely the cause of death. A simple x-ray of the cervical column, mainly in maximal flexion and extension on the lateral projection, is the most frequently employed diagnostic method to see a reduction in space. Radiographs can show no pathologic signs when there are neurological alterations or, on the contrary, a radiograph that shows an important AAS can appear in a patient without spinal cord affection. Magnetic resonance (MR) can measure with a higher degree of certainty the diameter, and can indicate the etiology of the compression (ie, if there is pannus). The affection of the spinal column detected through MR is a predictive factor for the deterioration of myelopathy in patients with RA, even in the absence of clinical signs. Somatosensory evoked potentials (SEP) and transcortical magnetic stimulation (TMS) are neurophysiological studies that can be useful for an early diagnosis of neurological damage. SEP study sensitive conduction that occurs mainly through the posterior columns and TMS studies motor conduction on the anterolateral columns. Normality of both tests signals to an integrity of the spinal cord, and have been shown to prove neuronal damage in patients with normal imaging testing. In the present study we compare the results of neurophysiological testing practiced on patients with RA, with or without AAS, with no neurological clinical symptoms or signs, thus evaluating the efficacy of early diagnosis of spinal cord affection by electrodiagnostic methods.

**Material and Methods**

Design: it is a descriptive study of a series of patient cases with RA of more than 3 years since onset; in this study we compared the characteristics of patients with AAS and those without it. Patients were selected from the rheumatology outpatient clinic who complied with the American College of Rheumatology 1987 criteria for the classification of RA. Patients were included as cases if they came to their visits in a regular manner and had a known diagnosis of AAS; for controls, patients who had RA but not AAS were included. All patients underwent a lateral cervical column radiograph. Patients in the study did not present motor deficits, alterations in the cranial nerves nor severe sensitive alterations or sphincter dysfunction. None of them presented a plantar extensor reflex. All patients belonged to group I of the Ranawat classification (Table 1).

<table>
<thead>
<tr>
<th>TABLE 1. Ranawat Classification</th>
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<tbody>
<tr>
<td>I. Patients without neurological deficits</td>
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<tr>
<td>II. Patients with paresthesias, hyper-reflexia, and subjective sensation of loss of strength</td>
</tr>
<tr>
<td>III. Patients affected by a motor deficit</td>
</tr>
<tr>
<td>IIIA. Possibility for moving</td>
</tr>
<tr>
<td>IIIB. Impossibility for moving</td>
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Determination of central motor conduction was done from an F wave method.

For the statistical analysis a SPSS for windows, version 11 was employed.

To determine the effect of each variable we employed non-parametric testing, Mann-Whitney U test for quantitative variables and χ² Fisher’s exact test for qualitative type variables.

**Results**

Twenty-nine patients participated in the study, 21 women and 8 men; 12 (9 women and 3 men) did not present AAS and 17 (12 women and 5 men) did.

Of patients with AAS, 11 (64.7%) had erosions, and 12 (70.5%), positive rheumatoid factor; of those without AAS, 8 (66.6%) presented erosive RA and 7 (58.3%) were seropositive (Table 2).

The mean distance (standard deviation) of AAS was 4.9 (1.7) mm and a range of 3-8 mm. Time since onset of RA oscillated between 3 and 35 years; on the other hand, age at onset went from 18 to 66 years.

The results from the electrophysiological testing were as follows: in the group with AAS, 2 (11.7%) patients presented an anomaly in SEP and 7 (41.1%), in TMS; with the particularity that the 2 patients which had an altered SEP were male and the 7 with the diminished TMS were women. In the group without AAS, 2 (16.6%) patients had an altered TMS and none had alterations in SEP. Therefore, 9/17 (52.9%) patients in the group with the particularity that the 2 patients which had an altered SEP presented AAS and were male (40% of males with AAS), something that was not altered in any woman. No differences were found between the neurophysiological alterations, years since onset of RA, age at presentation, positivity for RA, and the presence of erosions. No significant differences have appeared between the distance of the AAS and the neurophysiological manifestations.

**TABLE 2. Characteristics and Results From the Study**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>AAS (12)</th>
<th>Without AAS (17)</th>
<th>P</th>
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<tbody>
<tr>
<td>Women</td>
<td>12 (70.6%)</td>
<td>9 (75%)</td>
<td>.98</td>
</tr>
<tr>
<td>Erosions</td>
<td>11 (64.7%)</td>
<td>8 (66.6%)</td>
<td>.61</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>12 (70.5%)</td>
<td>7 (58.3%)</td>
<td>.69</td>
</tr>
<tr>
<td>Years with rheumatoid arthritis</td>
<td>12.9 (7.5)</td>
<td>9.5 (5.2)</td>
<td>.17</td>
</tr>
<tr>
<td>Age at onset</td>
<td>50.4 (12.6)</td>
<td>52.4 (8.2)</td>
<td>.79</td>
</tr>
<tr>
<td>SEP altered</td>
<td>2 (11.7%)</td>
<td>0</td>
<td>.49</td>
</tr>
<tr>
<td>TMS altered</td>
<td>7 (41.1%)</td>
<td>2 (16.6%)</td>
<td>.23</td>
</tr>
<tr>
<td>Total altered</td>
<td>9 (52.9%)</td>
<td>2 (16.6%)</td>
<td>.06</td>
</tr>
</tbody>
</table>

*Values expressed as mean (standard deviation) for continuous variables or n (%) for categorical variables. TMS indicates transcortical magnetic stimulation; SEP, somesthetic evoked potentials; SAA, atlantoaxial subluxation.

No significant differences between those positive for rheumatoid factor (RF) or the presence of erosions and atlantoaxial joint abnormalities were found.

There were no differences either between the age at onset or years since onset and AAS. As for the group of patients with electrophysiological abnormalities (SEP and TMS), there were differences, with no statistical significance, regarding gender, because 2 of the patients with an alteration in SEP presented AAS and were male (40% of males with AAS), something that was not altered in any woman. No differences were found between the neurophysiological alterations, years since onset of RA, age at presentation, positivity for RA, and the presence of erosions. No significant differences have appeared between the distance of the AAS and the neurophysiological manifestations.

**Discussion**

Because it is a study with a limited number of patients, results must be interpreted with caution, though they are similar to those described previously.

In our study, patients with AAS had a larger tendency to alterations of the neurophysiological studies than patients without AAS. SEP was normal in all of the patients without AAS and was altered in 2 of the patients with AAS. A slowing of the motor conduction was shown in 7 patients with AAS and also in 2 without AAS. No patients had both electrophysiological tests with alterations. All of our patients belonged to group I of the Ranawat classification; group II and beyond is associated with neurological symptoms that can indicate an alteration in the spinal cord; therefore, patients in group I are those that can benefit more from an early diagnosis. The study shows that 52.9% of patients with AAS have some neurophysiological alteration, compared to 16.6% of the group of patients without AAS; this difference is significant.

By carrying out 2 electrophysiological techniques we increased the sensitivity in diagnosis of neurological affection by AAS, because no patients presented alterations in both tests, though it is still to be determined if normality in both tests eliminated that possibility.

Some studies show neurophysiological testing as methods for the early detection of cervical neurological affection due to RA. It is important to reach an early diagnosis because clinical neurological signs appear late in the course of the disease and can overlap with other RA manifestations (interosseus muscle atrophy, peripheral neuropathy, hand rigidity, etc). We must keep in mind that all of the patients were asymptomatic at the moment of the study, both in the anamnesis of pain as in the physical examination directed to the detection of neurological deficits, both motor and sensitive.

We know that MR is the most specific method to evaluate cervical morphology, mainly in the spinal cord, and is very
sensitive to detect abnormalities in these zones, though it does not study the functionality of the neuronal pathways. Other diagnostic tests of cord lesions due to AAS can be tridimensional computed tomography of the cervical column and echo-Doppler of the supraaortic trunks in positions of extreme movement of the cervical column. Electrophysiologic tests do not substitute MR, and it is possible for both tests to be complementary and provide a better evaluation of the neuronal pathways, because one must take into account the fact that pathologic alterations can appear both in x-rays as in MR (including lesions of the spinal cord) without functional alterations, or vice versa; therefore, the radiological evaluation can be complemented by electrophysiological tests.

Neurological alterations can present themselves even when not caused by a subluxation (ie, spinal cord vasculitis, granulation tissue, synovial pannus, etc). An early diagnosis is desirable because treatment, both conservative and surgical, can improve the neurological clinical signs and reduce progression. We found no significant differences regarding gender, erosions, age at onset, years since onset of RA (which was discreetly higher in AAS, without achieving significance). Though we know that patients with AAS have more erosions and a higher prevalence for RF seropositivity in AAS affected and non affected patients, alterations and the distance of the AAS. Some authors have shown similar data of neurophysiological alterations in AAS affected and non affected patients, in contrast to others who do show a higher prevalence in patients with AAS, making the neurophysiologic tests for the diagnosis of AAS more specific, though less sensitive (similar to our results).

It is interesting to note that both of the patients that had an alteration in the SEP were male, because this fact has not been described previously though it could be due to the sample size or something random. In summary, we believe the fact of the appearance of neurophysiologic alterations in patients with AAS and RA without any clinical signs to be interesting. The difference in the prevalence of neurophysiological alterations between patients with and without AAS is clear, and it cannot be explained by other clinical or radiological variables. Though the sample is limited and no definite conclusions can be extracted, the results are in agreement with most of the previous studies.

References