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RESEARCH ARTICLE

Demographic characteristics, and the value of the split-hand phenomenon, as an early marker and prognostic of amyotrophic lateral sclerosis, in a Mexican reference hospital

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ABSTRACT

Introduction: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by motor neuron damage, with high comorbidities and in most cases fatal. We carried out a review of our Mexican hospital center on the performance of a neurophysiological index using the Abductor Pollicis Brevis / Abductor Digiti Minimi (APB/ADM) with cut-off values of less than 0.6, which is reproducible, sensitive and easy to perform in patients with suspected ALS, and at the same time, analyzes the correlation that this index has with the clinical scale of ALSFRS (Amyotrophic Lateral Sclerosis Functional Rating Scale).

Method: A retrospective cross-sectional study was carried out where a total of 26 patients who were admitted to the neurology department of a reference hospital in Mexico City were included, these patients met the inclusion criteria for a diagnosis of ALS according to El Escorial criteria, from January 2018 to June 2023.

Results: Of the total number of patients, 14 were women and 12 were men, the mean age was 57.4 with 95% CI (51-63), at the time of diagnosis the mean ALSFRS scale 31.4 with 95% CI (27.35-35.5). Indices were obtained in the APB/ ADM nerve conduction study as less than 0.6, which was positive in 22 patients and negative in 4 patients. In the statistical analysis, where neurophysiological and biochemical variables were tested using the Chi-square test, the only variables that demonstrated a significant difference were the APB/ADM index less than 0.6 with ALSFRS greater than 25, where a P=0.028 was obtained.

Conclusions: The split-hand index was found positive at the time of diagnosis in 84%, and showed a statistically significant relationship for both the APB / ADM index ratio less than 0.6 along with an ALSFRS scale score (>25) in our population, which could be a potential marker correlated with the functional rating scale of patients with ALS.

Keywords: split-hand, amyotrophic lateral sclerosis, neurophysiology.

Introduction

ALS is a degenerative and progressive disease that generally appears in adulthood and is characterized by the degeneration of upper or lower motor neurons[1]. Phenotypically it is characterized by muscle weakness, atrophy, fasciculations, spasticity and hyperreflexia[2,3]. Generally, the forms are sporadic but 5 to 15% of cases are identified as familial[4]. The worldwide incidence of ALS is approximately 3-6 cases per 100,000 inhabitants with a mean of the sixth decade of life[5]. The 2016 Global Burden of Diseases, Injuries, and Risk Factors Study described heterogeneous global incidence data for motor neuron diseases (0.36 to 2.77 cases per 100,000 person-years), with the highest rates in Asia-Australia, North America, and Western Europe, and the lowest in Africa and Central Asia[6]. ALS typically starts in the extremities and becomes generalized. Besides the classic ALS manifestations, less frequent variants have been described, including limited presentations affecting thoracic or pelvic limbs, respiratory or bulbar regions, and upper or lower motor neurons in pure form[7,8]. Data on the regional epidemiology and survival of patients with ALS in Mexico are relatively limited. Early diagnosis is crucial for providing appropriate care and improving survival, yet ALS patients often experience significant diagnostic delays[9]. The typical median time between initial symptoms and a definitive diagnosis is 10 to 16 months[10]. Survival rates post-diagnosis vary considerably. Several prognostic factors are known, including site of onset (bulbar or limb), age at symptom onset, delay from onset to diagnosis, and the use of riluzole and non-invasive ventilation (NIV)[11]. New classification and scoring systems may help monitor disease progression in ALS patients and could potentially serve as clinical trial outcomes[12].

Finally, new tools such as biofluid markers, imaging modalities, and neuromuscular electrophysiological measurements may increase diagnostic and prognostic accuracy[13]. The split-hand sign has been identified in ALS patients, indicating involvement of the cortical motor neuron. Tested muscles like the Abductor Pollicis Brevis (APB) or the First Dorsal Interosseous muscle (FDI) have extensive corticospinal connections affected by glutamate excitotoxicity. The split-hand sign has been identified in patients with ALS, which indicates involvement of the cortical motor neuron. The muscles tested, which are the Abductor Pollicis Brevis (APB) or the First Dorsal Interosseous muscle (FDI) have extensive corticospinal connections affected by glutamate excitotoxicity[14]. While the Abductor Digiti Minimi muscle (ADM) presents relative sparing because the affected cortical area is smaller[15], when performing nerve conduction studies, obtaining the amplitude of the PAMC in these muscles, these show a decreased APB/ADM amplitude ratio of the compound muscle action potential (CMAP) (< 0.6), which reflects the split-hand phenomenon. Therefore, part of our objective is to determine if these indices correlate with disease prognosis when obtained. Among the tools that are used to assess prognosis, there is the ALSFRS-R scale, which is an instrument to measure the progression of ALS. It consists of 12 items grouped into four fields that grade disabilities in daily activities. It is a widely accepted scale for monitoring functional level, in clinical practice and research. Several studies have validated the use of ALSFRS-R as a marker of disease severity, measurement of disease progression, and early

disease prognosis[15]. A total score exceeding 25 points has been associated with a greater than 60% probability of 9-month survival, indicating a better prognosis[16,17].

Thus, as an widely accepted and easily applicable scale, it will be used to explore the prognostic value of the APB/ADM index and therefore of the split-hand sign.

Methods

We carried out a cross-sectional, analytical and single-center study including electronic medical records of patients hospitalized in Neurology who met certainty diagnostic criteria of El Escorial diagnosis (probable and definitive) of amyotrophic lateral sclerosis from January 2018 to June 2023. The sample size calculation was convenient in the period of time described. Patients with incomplete medical records were excluded, as well as those with a diagnosis of cervical spondylotic myelopathy (CSM), peripheral neuropathies, regional variants of ALS, and patients with disease progression of more than 12 months. Demographic characteristics, initial symptoms, time of evolution, symptoms at the time of evaluation, functional outcome, and variables of the nerve conduction studies were described, in the latter, the APB/ADM index < 0.6 was determined, which is what is described as the sign of split-hand. Patients who presented the positive index for split-hand were assigned into 2 groups: good or poor prognosis according to the ALSFRS clinical scale score (in > 25 points good prognosis and < 25 poor prognosis).

Statistical Analysis

For the statistical analysis, the IBM SPSS program was used. To determine the normality of the sample and data distribution, the Shapiro-Wilks test was used. For the descriptive analysis, the variables are presented with median and interquartile range according to their distribution. Categorical variables were described in frequencies and percentages. To identify differences among groups, the Chi-square test was used for non-parametric variables. P ≤ 0.05 was considered statistically significant.

Results

26 patients were included. Of the total, 14 were women (53.84%) and 12 were men (46.16%), the mean age was 57.4 with 95% CI (51-63). The average evolution time was 8 months. By symptoms onset according to anatomical site, the most frequent pattern was distal (61%), followed by proximal (36%) and bulbar (3%). At the time of diagnosis, the mean score on the ALSFR scale was 31.4 with 95% CI (27.35-35.5). The APB (Abductor Pollicis Brevis) / ADM (Abductor Digiti Minimi) index lesser than 0.6 was reported positive in 22 patients (84.6%) and negative in 4 patients (15.4%). There were no differences in terms of gender, affected initial segment correlated with ALSFRS. In the bivariate analysis, a statistically significant relationship was demonstrated for both the ACP/ADM index ratio less than 0.6 along with an ALSFRS scale score (>25) p=0.028; but no significant correlation was shown between the site of symptom onset according to the anatomical region and the ALSFRS clinical scale score (>25) p=0.386.

Discussion

In the present systematic review, we summarize the results to show the frequency of split-hand in patients with ALS, discarding atypical forms,

at the time of diagnosis and to know if there is a correlation between the positivity of the index and the clinical severity of the patient.

Our results showed the ratio of patients with ALS was almost 1:1 of men and women, which is what is established in the international medical literature, where the incidence is 1:1.35[18]. It was observed that the evolution time for disease diagnostic was 8 months, within our country differs a little from other studies in the region, but it is similar to what other authors have reported in a range of 8 to 15 months[19]. The mean age of onset in our study is of 57.4 years, similar to the global correlation, this varies greatly according to the literature, the region and the ancestral background of the area[20]. A higher incidence of the disease has been found between 60 and 80 years of age, and as these increases as the population ages[21], at the time of carrying out the diagnosis of ALS in our population, we found the positivity index less than 0.6 in 22 patients (84.6%) and negative in 4 patients (15.4%). In other series this data differs a little, since in a meta-analysis with 339 patients, it was shown that only 50% of patients have a positive index[22]; in studies of smaller series that included 9 and 10 cases, a slightly lower frequency was reported, 70% and 66.6% respectively[23,24]. This may be associated in our population due to the anatomical pattern most affected initially was the distal as well as the thoracic limbs. Within the neurophysiological findings, the split-hand phenomenon is defined as a difference between the APB/ADM CMAP amplitude ratio (<0.6). In our study, it was reported positive in 22 patients (84.6%). In the initial studies, a positive relationship of this index was mentioned in 41% of patients with ALS and in 5% of patients without the disease, this correlation is much broader in our study. We found no correlation between the positivity of the index in terms of gender or the initially affected segment. At the time of diagnosis, our patients had on average a high score on the function scale (ALSFRS >25 points), in the bivariate analysis we found a statistically significant correlation between the positive APB/ADM index (less than 0.6). It is important to mention that the split-hand phenomenon is best found within the first 12 months of symptom onset since there is still no noticeable atrophy that would reduce the positivity of the index. By this, we emphasize that it is an important electrophysiological finding in the initial stages of the disease and is related to a high score and important involvement in the functionality of the patient with ALS. Finally, we must point out that it is well known that this index can be related to other forms of motor neuron disease, so it cannot be classified as exclusive to ALS, therefore, the appropriate clinical connotation must be given.

Conclusions

The split-hand index was initially developed as a biomarker that allows us to differentiate motor neuron disease from other etiologies in early stages. It has been found in studies that the noticeable reduction of this index is related to greater loss of functionality at the level of the lower motor neuron, greater severity and progression of the disease. Although more studies are necessary to elucidate the exact correlation of this index with the burden and severity of the disease, it has the potential to be a clinical biomarker to determine the outcome and functional prognosis of the disease due to its ease of replicability.

Conflict of Interest Statement:

None

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