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Value of protein concentration in cerebrospinal fluid in paediatric patients with Guillain–Barre syndrome☆

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ABSTRACT

Introduction and objective: The albumin-cytologic dissociation in cerebrospinal fluid (CSF) supports the diagnosis of Guillain–Barre syndrome (GBS) but does not support the prognosis, so the aim of this study is to determine the usefulness of protein numbers in the CSF to predict progression in pediatric patients.
Patients and methods: A diagnostic test was performed in pediatric patients with GBS, analysing sociodemographic, clinical and protein variables in CSF as well as electromyography. The presence of dysautonomia was also documented.
Results: Data were analyzed from 23 patients, predominantly males (87%), school age (43.5%) and history of digestive infection (73.9%). Using the ROC curve, an area under the curve of 0.966 with best CSF protein cut-off point of 87–92 proteins/mm was found for the presence of dysautonomias and to evaluate the poor response to treatment with 0.969 intravenous immunoglobulin with better cut-off point in 157 proteins/mm.
Conclusion: The amount of proteins in the CSF can be used as a prognostic indicator and severity, such that proteins greater than 100 in CSF translate into a torpid evolution and with greater complications.
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Valor de la concentración de proteínas en el líquido cefalorraquídeo en pacientes pediátricos con síndrome de Guillain-Barré

Palabras clave:
Síndrome de Guillain-Barré
Proteínas
Líquido cefalorraquídeo
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RESUMEN

Introducción y objetivo: La disociación albuminocitológica en el líquido cefalorraquídeo (LCR) apoya el diagnóstico de síndrome de Guillain-Barré (SGB) pero no ayuda en el pronóstico, por lo que el objetivo de este estudio es determinar la utilidad de las cifras de proteínas en el LCR para predecir la evolución en pacientes pediátricos.
Pacientes y métodos: Se realizó un estudio de prueba diagnóstica, en pacientes pediátricos con SGB, analizando variables sociodemográficas, clínicas y proteínas en LCR, así como electromiografía; también se documentó la presencia de disautonomías.
Resultados: Se analizaron datos de 23 pacientes, predominando el sexo masculino (87%), la edad escolar (43,5%) y el antecedente de infección digestiva (73,9%). Mediante la curva COR se encontró, para la presencia de disautonomías, un área bajo la curva de 0,966 con mejor punto de corte de proteínas en LCR de 87-92 proteínas/mm, y para evaluar la pobre respuesta al tratamiento con inmunoglobulina intravenosa, de 0,969, con mejor punto de corte en 157 proteínas/mm.
Conclusión: La cantidad de proteínas en el LCR puede utilizarse como un indicador pronóstico y de gravedad, de tal manera que unas proteínas mayores de 100 en el LCR se traducen en una evolución tórpida y con mayores complicaciones.
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Introduction

Guillain–Barre syndrome (GBS) is a disease mediated by autoimmunity and molecular mimicry, characterized by a cellular and humoral response against peripheral nerve myelin. Clinically, it manifests as weakness in the lower limbs, back pain, sensory and/or motors symptoms with ascending progression and diminished or absent tendon reflexes; occasionally, the cranial nerves (facial, bulbar, and oculomotor) are affected and up to 25% of patients require mechanical ventilation.[1–3]

Albuminocytological dissociation in cerebrospinal fluid (CSF) and abnormal nerve conduction velocity in the electromyography support the diagnosis, although most patients with GBS may not present CSF alterations in the first 48 h, but 90% have elevated proteins in the second week, without pleocytosis (leukocytes <10 mm^3).[4,5]

The treatment of GBS includes intravenous immunoglobulin (IVIg) and plasmapheresis. Studies on the effects of these treatments on the prognosis of the disease show that patients treated with IVIg have a better prognosis; other studies show that plasma exchange performed in the first 7 days shortens the disease course.[6–8]

Little has been studied about the amount of proteins in the CSF and its association with the progression and presence of complications. The only utility given to the CSF cytology study is the albuminocytologic dissociation as such, without conferring value to the quantitative study, so the objective of this study is to determine the usefulness of protein concentration in CSF as a predictor of progression in pediatric patients with GBS.

Patients and methods

A study was carried out with a diagnostic test evaluation design, in records of pediatric patients with GBS diagnosed between January 2013 and October 2015.

The patients were admitted by the Emergency Department to a secondary-level hospital, where the diagnosis was made based on the clinical criteria described by Erazo,[5] and the CSF cytological study on the seventh day after the onset of symptoms, where the presence of albuminocytologic dissociation was corroborated, which is defined as the increase of CSF proteins with normal cellularity. The CSF study was carried out by centrifugation, separating and mixing the components with 20% albumin in order to preserve cellular morphology and integrity during the smear, in which a count of the different cells is carried out.

These patients also underwent an electromyography to confirm the neuropathic condition. This last study was carried out between week 2 to one month of progression; 2 electrodes were used to register the response, which were placed, after skin asepsis, in direct contact with the muscle or nerve; a stimulus was applied in an increased-strength manner until reaching a maximum and until 3 parameters were recorded: distal latency (time between stimulus and response), velocity and characteristics of the evoked potential (shape, amplitude, duration and area).

In order to detect dysautonomies, blood pressure was measured using the auscultatory method, considering a normal blood pressure when the systolic and/or diastolic pressure levels were lower than the 90th percentile, as hypertension, those greater than the 95th percentile and as hypotension, those under the 3rd percentile according to age. Heart rate was also measured; the figures obtained were recorded in one of the following categories according to age, considering 60–140 bpm as normal levels in 4–10-year-old children and 60–100 bpm in those older than 10 years of age, levels above or below these were considered tachycardia and bradycardia, respectively. These were assessed daily and reported whenever they occurred. Muscle strength was also assessed using the Daniels's scale.[9] As a treatment, they received IVIg for 5 days, in doses of 400 g/kg/day; none received steroids or plasmapheresis.

The project was authorized by the local research and ethics committee of the unit in which the study was conducted, with the parents' written informed consent

Results

We analyzed data from 23 pediatric patients who had flaccid paralysis, confirmed as GBS, between January 2010 and October 2015. 5 cases were excluded due to the absence of electromyographic confirmation. So, 23 cases were analyzed in total, with male predominance (20, 87%). In relation to age, the most prevalent group was that of school children, which included 6–12-year-old patients, with 10 cases corresponding to this group, representing 43.5%, followed by preschool children with 7 (30.4%) and adolescents with 6 (25.2%). As for the area of residence, 19 (82.6%) came from urban areas and 4 (13%) from rural areas.

In relation to the type of presentation, 21 (91.3%) had the typical one and 2 (8.7%) had the Miller–Fisher[9] variant; 2 weeks before the episode, the history of infection was respiratory in 6 cases (26.1%) and digestive in 17 (73.9%).

The most frequent signs and symptoms were weakness (23; 100%) and areflexia (23; 100%), followed by pain in the lower limbs (16; 69.3%), headache (7; 30.4%) and paresthesias (3; 13%).

The complications were added infections (sepsis, urosepsis, soft tissues) in 8 (34.8%), nosocomial pneumonia in 6 (26.1%) and pneumothorax in one case (4.3%), with null mortality. The dysautonomies that occurred were hypertension in 11 (47.8%) and tachycardia in 11 (47.8%), followed by hypotension in 2 cases (8.7%).

In relation to the analysis of proteins in the CSF, in 9 cases (39.1%) a count of 51 to 100 was obtained, followed by 6 cases (26.1%) that had a count higher than 150, 5 (21, 7%) between 101–150 and 3 (13%) less than 50.

When applying a correlation analysis, it was found that the amount of proteins in the CSF has a directly proportional relationship with the occurrence of dysautonomies and with a torpid progression, in such a way that among patients who have a spinal fluid protein concentration in the range of 101–150 proteins, 80% had dysautonomies (tachycardia and hypertension), increasing this percentage to 100% in those whose CSF protein concentration was higher than 150.

Clinical improvement was also found with the IVIg treatment, with recovery of strength at the third dose in 9 cases (39.1%), at the fourth dose in 2 cases (8.7%) and at the fifth dose in one case (4.3%); with none after the 2 initial doses. After the administration of IVIg, a clinical improvement was observed in all patients who had a protein concentration lower than 100 cells, among the patients with a spinal fluid protein concentration of 101–150, only 5 cases (20%) showed improvement, while none of the patients with protein concentrations above 150 showed any improvements.

In relation to requiring assisted mechanical ventilation, it was observed that 5 (83%) patients with CSF protein concentrations above 150 required it, 3 (50%) of them for more than one month (Table 1 Table 1).

Table 2 shows the relationship between the electromyography data and the days of stay in the Intensive Care Unit; in the latter, a longer stay was observed when the spinal fluid protein concentration were higher (above 30 days in 33.3%), however, the difference is not statistically significant; complications occurred more frequently in patients with spinal fluid protein concentration higher

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