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ADVANCES IN THE DIAGNOSIS AND TREATMENT OF GUILLAIN-BARRÉ SYNDROME: INSIGHTS FROM 2023

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Abstract: Objective: Evaluate and synthesize the most recent advances in diagnostic criteria, biomarkers, treatments, rehabilitation strategies, and long-term follow-up for Guillain-Barré Syndrome, with the aim of determining the impact of these updates on the prognosis and recovery rates of patients. patients affected by this condition. Methods: Narrative bibliographic review study, using the Pubmed database. A search was carried out using the research strategy: (Guillain Barre Syndrome) AND (Management) AND (Diagnosis). Initially, 263 articles were found, of which 20 were selected after applying inclusion and exclusion criteria. Review: The advances in the diagnosis and treatment of GBS, highlight the importance of specific biomarkers, such as metallo-proteinases (MMP-2), vascular endothelial growth factor (VEGF), sphingomyelin (SM), pre-albumin, fibrinogen and haptoglobin and in analysis identification of unfavorable lipid profiles in early diagnosis. Furthermore, traditional therapies, such as Human Immune Globulin (IVIG) and Plasmapheresis (PE), present efficacy in treatment, but also the associated risks, also highlighting the need for an abcustom order and the lack of other available alternatives. **Final considerations:** The importance of early diagnosis and treatment of Guillain Barré Syndrome (GBS) was highlighted, directly impacting the patient's prognosis and being able to avoid any permanent axonal injury in patients with severe conditions and risk factors. Highlighting the lack of research focused on understanding the pathological mechanisms of GBS, enabling the development of other therapies that could provide a better prognosis.
Keywords: Guillain-Barré syndrome, immunotherapy, diagnosis, treatment.

INTRODUCTION

The Guillain-Barré Syndrome (GBS) is an acute inflammatory polyradiculoneuropathy where the immune system attacks the peripheral nervous system. Manifesting with clinical symptoms that vary between patients, the most common include progressive muscle weakness and areflexia (Shahrizaila, Lehmann and Kuwabara, 2021). GBS has several subtypes with distinct characteristics: acute inflammatory demyelinating polyradiculoneuropathy (AIDP), the most prevalent form characterized by demyelination and inflammation of peripheral nerves; acute motor axonal neuropathy (AMAN), which directly affects axons without significant demyelination or inflammation (Yao, Zhou, Liu, & Lu, 2023); Miller-Fisher Syndrome, recognized by ataxia, areflexia and ophthalmoplegia (Kwan and Biliciler, 2021); and acute sensorimotor axonal neuropathy (AMSAN) described by Leonhard et al. (2019).

The GBS is relatively rare, with an incidence of approximately one case per 100,000 people per year, with a higher risk in men and a 20% increase in incidence for each decade of life, especially in older adults. The condition is often associated with risk factors related to immune responses to infections in the previous four weeks, with agents such as Campylobacter jejuni, the hepatitis E viruses, Zika, Epstein-Barr, influenza A and B and, more recently, SARS-CoV -two. Rare cases associated with vaccination against influenza A (H1N1) have also been documented (Shahrizaila; Lehmann; Kuwabara, 2021).

According to Leonhard et al. (2019), the progression of GBS is rapid, with patients reaching maximum disability on average two weeks after the onset of symptoms. This progression significantly affects quality of life, from the acute phase to long-term recovery and rehabilitation. Despite access to adequate professional care, mortality is estimated at

between 3 and 10% of patients, while 60 to 80% are able to walk independently six months after the onset of symptoms, with or without treatment. Specific mortality is around 5%, and around 20% of patients do not walk independently again one year after the onset of the disease, even with standard treatment (Shahrizaila, Lehmann, and Kuwabara, 2021).

Despite significant challenges in the management of GBS, such as severe complications and rapid progression, advances in diagnostic criteria have contributed to an improved prognosis. Limitations continue to be a challenge, with a relevant percentage of patients unable to walk after the syndrome, indicating a negative influence on quality of life. Therefore, it is crucial to continue investigations to deepen understanding of the underlying mechanisms of GBS, develop more effective treatments with fewer side effects, and improve rehabilitation strategies. The future landscape for GBS treatment may include personalized therapies based on individual disease characteristics and more accurate biomarkers, as well as integrating new rehabilitation and remote monitoring technologies to provide ongoing support to patients. With the constant updating of new diagnostic methods and improvements in prognosis in the neurological area, it is essential to analyze current studies to reflect on their practical implications for patient care, facilitating neurological clinical practice and future treatments for GBS.

METHODOLOGY

Narrative bibliographic review developed according to the criteria of the PVO strategy, an acronym that represents: population or research problem, variables and outcome, which was used to prepare the research through the guiding question: "What are the main advances in diagnostic criteria and treatments for Guillain-Barré Syndrome (GBS) by 2023, and how do these impact the prognosis and recovery rates of patients?"

The searches were carried out through searches in the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) database. The Boolean term "AND" was used through the search strategy: (Guillain Barre Syndrome) AND (Management) AND (Diagnosis). From this search, 263 articles were found, subsequently submitted to the selection criteria. The inclusion criteria were: articles in the English language, published in the last 5 years, review-type studies, meta-analysis, observational studies, such as case-control studies and cohort studies, and clinical trials, which addressed the themes proposed for this research and which were made available in full. The exclusion criteria were: duplicate articles, available in abstract form, which did not directly address the proposal studied and which did not meet the other inclusion criteria. After applying the inclusion and exclusion criteria, 20 articles were selected from the PubMed database to compose the study collection.

DISCUSSION

The Guillain-Barré Syndrome (GBS) presents as an acute immune-mediated peripheral neuropathy, whose symptoms typically begin with ascending and symmetric paresis, reaching a peak between 3 and 15 days. Most patients experience remission of symptoms within four weeks (Wang et al., 2023). Although the exact pathogenesis of GBS is not yet completely elucidated, studies suggest that the immune response may be associated with the activation of the complement system and T cell cytotoxicity, in addition to involving a complex cytokine system in mediating the inflammatory response (Li et al., 2023; Papri et al., 2021). The latter has shown a significant positive predictive value in the differential diagnosis between GBS and chronic inflammatory demyelinating

polyneuropathy (CIDP).

Recent studies have highlighted the importance of specific biomarkers, such as metalloproteinases (MMP-2) and vascular endothelial growth factor (VEGF). These biomarkers were found in high concentrations in the cerebrospinal fluid of patients with GBS and CIDP, suggesting their potential usefulness in diagnosing the disease (Oeztuerk et al., 2023; Dash; Kamath; Pai; Rao, 2022). Furthermore, Capodivento et al. (2021) identified sphingomyelin (SM) in cerebrospinal fluid as a promising biomarker for the early identification and classification of neuropathies, helping to distinguish between CIDP and GBS.

Other biomarkers, such as prealbumin, fibrinogen and haptoglobin, were also investigated.

Prealbumin and fibrinogen levels in the CSF of patients with GBS were lower than in patients with non-inflammatory neurological conditions, while haptoglobin levels were not elevated in patients with GBS, but were increased in cases of multiple sclerosis. (EM) and PIDC (Zhang et al., 2012).

A study by Chang et al. (2007) pointed to haptoglobin as a useful diagnostic biomarker in GBS, although its elevated levels do not correlate with the severity of the disease, limiting its use to diagnosis rather than prognosis.

Recently, Wang et al. (2023) highlighted that the lipid profile of patients with GBS differs significantly, with high levels of Apolipoprotein B (APOB), Apolipoprotein C2 (APOC2), Apolipoprotein C3 (APOC3), Apolipoprotein E (APOE), triglycerides (TG) and residual cholesterol (CR). These findings suggest that low-fat dietary interventions or the use of lipid-lowering medications may be beneficial during the treatment of GBS.

The classic treatment of Guillain-Barré Syndrome (GBS) involves the use of Human Immunoglobulin (IVIG) or Plasmapheresis (PE). These therapies must be applied as early as possible, before the development of any permanent axonal damage and in patients with severe conditions. PE is performed in 5 sessions of 50 ml/kg/session over 2 weeks, while the typical dose of IVIG is 0.4 g/kg/day for 5 consecutive days. Although the exact mechanisms of these treatments are unknown, it is believed that both acts to remove antibodies from plasma and modulate the immune response (Yao; Zhou; Liu; Lu, 2023; Verma et al., 2013).

Fokkink et al. (2022) and Zaki et al. (2023) highlighted that IVIG is preferred because it is easier to administer and is more widely available, despite being associated with a considerable number of deaths and serious complications. About 25% of treated patients may develop respiratory failure and 10-20% remain disabled after treatment. The choice of treatment must be cautious, as IVIG requires availability of intensive care units. Furthermore, the effect of IVIG on albumin is not yet known.

The efficacy of IVIG is dose dependent and its pharmacokinetics vary significantly between patients. Studies indicate that accelerated IVIG consumption is associated with more severe clinical conditions and a worse prognosis. Patients who maintain IgG levels above 7.3 g/L for at least two weeks after treatment tend to have better clinical outcomes (Fokkink et al., 2022; Yao, Zhou, Liu, and Lu, 2023).

Plasmapheresis, in turn, presents risks of complications such as thrombosis, pneumothorax, hypokalemia and allergic reactions, and is not recommended in cases of autonomic dysfunction. In mild to moderate cases of GBS, the use of IG and PE is generally not recommended due to the self-limiting nature of the disease and the associated high cost and risk (Verma et al., 2013).

Shastri, Aiyan, Kishore and Farrugia (2023) observed that patients' progress can worsen soon after an initial breakthrough, highlighting the importance of complementary therapies such as physiotherapy, neurorehabilitation and psychotherapy for an effective recovery.

Additionally, studies suggest that patients receiving PE may have a shorter hospital stay and reduced need for mechanical ventilation (Mohy-Eldeen; Ahmad; Mahran; Saad, 2020).

New therapies involving antibody Fc receptor (FcRn) inhibitors have shown potential in animal studies, reducing nerve cell damage and associated symptoms. These results point to the possible future use of these inhibitors in modulating IgG levels and treating GBS (Yao; Zhou; Liu; Lu, 2023).

Leonhard et al. (2019) highlighted that patients with quadriplegia or who required prolonged mechanical ventilation showed significant improvement, especially in the first year, with around 80% of patients returning to walking without support in the first six months. However, 3-10% of cases result in death due to cardiovascular and respiratory complications. Residual symptoms such as pain, weakness and fatigue are common, but most patients show potential for recovery within five years. Recurrence of GBS is rare, occurring in approximately 2-5% of cases, making it crucial to carefully evaluate the vaccination schedule and its contraindications.

Papri et al. (2021) highlighted that the treatment of GBS requires a multidisciplinary approach, including medical support and immunotherapy. However, the benefits of these therapies are most evident in high-income countries, and can vary significantly in low- and middle-income countries. The ability to predict which patients will develop respiratory failure or have a poor prognosis would be highly beneficial, allowing for more targeted medical interventions. To this end, the Erasmus GBS Respiratory Failure Score (EGRIS) and the Erasmus GBS Outcome Score (EGOS and mEGOS) were developed to help predict the need for mechanical ventilation and long-term prognosis, respectively. However, these scores have been validated mainly in European populations, and studies in northeastern Brazil suggest that they may not be applicable to all populations (Papri et al., 2021).

Furthermore, as highlighted by Yao, Zhou, Liu and Lu (2023), advances in understanding the pathological mechanisms of GBS have led to the development of new therapeutic strategies. These include therapies targeting antibodies, complement system pathways, inflammatory cells and other specific mechanisms, promising a more effective and personalized approach to treating the disease.

FINAL CONSIDERATIONS

The importance is highlighted early diagnosis of this pathology and the evaluation of specific biomarkers, such as metalloproteinases (MMP-2), vascular endothelial growth factor (VEGF), sphingomyelin (SM), pre-albumin, fibrinogen and haptoglobin. Furthermore, the identification of distinct unfavorable lipid profiles in these patients also proved to be relevant during the investigation of GBS. Furthermore, in relation to treatment, therapies with human immunoglobulin (IVIG) and plasmapheresis (PE) were highlighted, which currently represent the classic treatment for GBS, but must be chosen cautiously, as they present a high risk of complications and considerable number of deaths, especially in patients with rapid progression. The results highlight the relevance of research that seeks to deepen the understanding of the pathological mechanisms of GBS, thus making it possible to develop alternatives for the treatment of this disease, such as new therapies involving inhibitors of antibody Fc receptors (FcRn), which have been being studied in

animals, pointing to a possible future use of these inhibitors in modulating IgG levels and treating GBS, promoting continuous innovation. In addition to highlighting the impact of a personalized multidisciplinary approach with complementary therapies such as physiotherapy, neurorehabilitation and psychotherapy, representing a significant factor for an effective recovery.

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