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Original article

Benefit in long-term response and mortality of treatment with intravenous immunoglobulin prior to plasmapheresis in peripheral polyneuropathies

Effets positifs sur les réactions à court terme d'un traitement des maladies neurologiques auto-immunes par immunoglobuline intraveineuse avant l'échange plasmatique

I. Parra-Salinas [a,*], V.P. González-Rodríguez [a], J.A. Gracia Pina [a], J.J. Gimeno Lozano [a], J.A. García-Erce [b]

[a] *Department of Hematology and Haemotherapy, Miguel Servet University Hospital, Paseo Isabel la Católica, 1-3, 50009 Zaragoza, Spain*
[b] *Department of Haematology and Haemotherapy, San Jorge Hospital, Av. Martínez de Velasco, 36, 22004 Huesca, Spain*

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Abstract

Objectives. – The benefits of plasmapheresis (PA) for neurologic autoimmune diseases have been widely demonstrated. Little is known about the long-term neurologic prognosis and course after PA and immunosuppressive (IS) and/or intravenous immunoglobulin (IVIG) treatment. We aimed to analyse features associated with short-term response and long-term outcome and prognosis (neurologic status and mortality) of peripheral polyneuropathy (PP) and central nervous system acute inflammatory disease (CNSAID) treated with PA.
Patients and methods. – A descriptive, retrospective single-centre study from January 2005 to December 2012.
Results. – There were 26 episodes, which included 16 CNSAID and 10 PP cases. First line therapy included PA ($n=4$), IS drugs ($n=15$), and IVIG ($n=7$). Responses were achieved in 80% and 50% of PP and CNSAID cases, respectively. For PP, first line treatment with IVIG and no IS treatment prior to or during PA were variables associated with short-term response ($P=0.067$), good or stable neurologic status at the end of follow-up ($P=0.008$), and lower mortality rate ($P=0.008$). For CNSAID, initial EDSS score ≥ 7 ($P=0.019$) was related to long-term good or stable neurologic status. During the study period, 177 sessions were conducted; 3.4% had technical complications and 8.5% clinical complications. However, these incidents were all minor and no PA session had to be discontinued.
Conclusion. – The response rates achieved in our patients were similar to those of other research. PA has a safe profile but double-blind, controlled studies are needed to evaluate the synergy of sequential treatment with IGIV followed by PA and the possible benefit for long-term outcome.

Keywords: Devic syndrome; Guillain-Barré syndrome; Multiple sclerosis; Plasmapheresis

Résumé

Introduction. – Les effets positifs de l'aphérèse plasmatique (AP) dans le traitement des maladies neurologiques auto-immunes sont largement démontrés. Le pronostic et l'évolution neurologique à long terme après un traitement par AP et immunosuppresseurs dans ce domaine sont très mal connus.
Objectifs. – Analyser les aspects associés aux réponses à court terme et à l'effet à long terme (statut neurologique et mortalité) du traitement par AP des polyneuropathies périphériques (PP) et de maladies inflammatoires aiguës du système nerveux central (MIASNC).
Patients et méthodes. – Étude descriptive, rétrospective et monocentrée (janvier 2005–décembre 2012).
Résultats. – Vingt-six épisodes : 16 MIASNC et 10 PP. Traitement de première intention : AP ($n=4$), traitement par immunosuppresseurs (IS) ($n=15$) et immunoglobuline intraveineuse (IgIV) ($n=7$). Pour des cas de PP, le traitement de première intention par IgIV sans traitement par IS préalable ou parallèle à l'AP étaient des variables associées à une réponse à court terme ($p=0{,}067$), un statut neurologique bon ou stable à la fin du suivi ($p=0{,}008$) et un taux de mortalité inférieur ($p=0{,}008$). Pour les cas de MIASNC, un score EDSS initial ≥ 7 ($p=0{,}019$) était associé à

* Corresponding author.
E-mail address: ingrid.mps@gmail.com (I. Parra-Salinas).

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un statut neurologique bon ou stable sur le long terme. Durant cette période, 177 sessions ont été conduites, 3,4 % desquelles ont rencontré des complications techniques et 8,5 % des complications cliniques, toutes bénignes, et n'ayant impliqué aucune interruption de l'AP.
Conclusions. – Les réponses d'ensemble atteintes par notre série sont semblables à d'autres recherches. L'AP offre un profil sûr mais des études à double insu contrôlées seront nécessaires à l'évaluation de la synergie d'un traitement séquentiel par IgIV suivi d'une AP, et les effets positifs possibles sur des résultats à long terme.

Mots clés : Maladie de Devic ; Syndrome de Guillain-Barré ; Sclérose multiple ; Aphérèse plasmatique ; Immunoglobuline intraveineuse

1. Introduction

Plasmapheresis (PA), immunomodulators, and/or immunosuppressants are recommended for the treatment of neurologic autoimmune diseases by different scientific bodies, such as the Spanish Neurological Society [1], American Academy of Neurology [2], American Society for Apheresis/American Association of Blood Banks (ASFA/AABB) [3], European Federation of Neurological Societies [20], Spanish Agency of Medicines, European Medicines Agency, and the United States Food and Drug Administration. Each disease has different therapeutic indications and varying levels of scientific evidence for treatment with these drugs or with PA. However, most general guidelines strongly recommend these as a first line of treatment [1–5].

The benefit of PA in this area has been widely demonstrated, mainly by clinical series and clinical practice guidelines [1–3,7–9], given that controlled and randomised meta-analyses remain scarce [4–6]. Despite the aforementioned scientific evidence, some authors still recommend PA as a second line therapy owing to its supposed poor tolerance, higher cost, and adverse effects; this means that PA is an underused therapeutic strategy. As mentioned by Papadopoulos et al., the limited indications for performing this technique are likely owing, in part, to a lack of randomised clinical trials and not because the results of such trials have been inconclusive [6].

Little is known in this field about long-term prognosis and course after PA and immunosuppressive/immunomodulatory therapy. The aim of this work is to analyse the clinical, laboratory, and radiographic features associated with short-term response and long-term outcome and prognosis (with respect to neurologic status and mortality) of PA in patients with peripheral polyneuropathy (PP) and central nervous system acute inflammatory disease (CNSAID).

2. Patients and methods

This work is a descriptive, retrospective, single-centre study at a level-four university hospital that is a referral centre for therapeutic aphaeresis techniques. Data collection was done by reviewing prospective records using a worksheet of the hospital transfusion service, clinical histories, and hospital medical records for all patients with PP and CNSAID who underwent PA treatment at our service between January 2005 and December 2012.

CNSAIDs in this study included Devic's disease, multiple sclerosis, transverse myelitis, and rhombencephalitis; PPs included Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy (CIDP), acute motor axonal neuropathy (AMAN), and Miller-Fisher syndrome.

2.1. Variables

The study unit was the clinical episode (sessions performed with a patient with the same therapeutic indication). Clinical evaluation was made using internationally recognised neurological disease scales: the Hughes GBS Disability Scale for PP and the Expanded Disability Status Scale (EDSS) for CNSAID.

2.2. Response

We identified four types of response. High functional improvement (HFI) was indicated by a decrease of ≥ 2 points on the Hughes scale or ≥ 1 point on the EDSS. Moderate functional improvement (MFI) was defined as a reduction of ≥ 1 point on the Hughes scale or ≥ 0.5 points on the EDSS. Stable deficit was indicated by no changes on the scale, and deterioration by an increase ≥ 1 point on the Hughes sale or ≥ 0.5 points on the EDSS. To facilitate statistical analysis, we defined good response as the sum of patients with HFI and MFI, and the remaining patients were classified as having no response.

2.3. Procedure

Blood tests (haemogram and biochemistry and coagulation tests) were carried out before and after each PA session. Autoimmune and serological testing were also done before the first session. Continuous flow cell separators (COBE Spectra® or Spectra Optia®) using a double light tunneled catheter were used. Patient clinical data and blood test results were recorded on the worksheet at the start of each procedure. Vital signs were recorded every 30 minutes, as were technical data and complications. The volume of plasma treated was 1–1.2 times the patient's total plasma volume, and anticoagulant citrate dextrose solution (ACD-A) was used. To avoid symptoms of hypocalcaemia, 20 mL of 10% calcium gluconate was administered intravenously at the beginning of the procedure and repeated if symptoms are detected. The fluid replacement solution was human albumin Grifols® 5%. After completing the procedure, 10 mL of vitamin K was administered intravenously. The number of sessions was those recommended by