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Immunoadsorption with regenerating systems in neurological disorders – A single center experience

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Abstract

In recent years, immunoadsorption is increasingly recognized as an alternative treatment approach replacing therapeutic plasma exchange in a variety of neurological disorders. While most experience is based on the application of single-use tryptophan adsorbers, less data exists on the application of more efficient regenerating adsorber columns. We here report the systematic use of a regenerating adsorber system in various neurological indications such as multiple sclerosis, encephalitis, myasthenia gravis and chronic inflammatory demyelinating polyneuropathy, providing the expected treatment success in regard to reduction of immunoglobulins and antibody clearance, together with a low rate of adverse events. As it has been shown for single-use columns before, immunoadsorption with regenerating adsorbers can be successfully applied in disorders without known specific antibodies such as multiple sclerosis. Regenerating systems offer the perspective to provide a more efficacious long term treatment perspective for such patients.

Keywords: Neurology; Multiple sclerosis; Immunoadsorption; Plasma exchange

1. Introduction

Extracorporeal treatments such as therapeutic plasma exchange and immunoadsorption (IA) have been considered as an treatment approach for a variety of neurological disorders [1]. While therapeutic plasma exchange is still the far most used technique to eliminate pathophysiologically relevant autoantibodies, several studies suggested at least equal potency of IA in such situations [2]. With a still rising number of newly detected autoantibodies in several neurological disorders, the extracorporeal treatment approach might become increasingly relevant, especially in acute, but also chronic situations. Based on the plasma exchange approach, most studies using IA so far tested single use tryptophan adsorbers and frequently stuck to a limited treatment number of 5 sessions. Meanwhile newer multi-use, regenerating adsorbers with a higher plasma treatment capacity have been invented. We have started the application of a regenerating system to treat autoimmune disorders at our apheresis center and here report our experience at a single center level.

2. Material and methods

This analysis included patients treated between September 2010 and July 2014 at the extracorporeal treatment and apheresis center at the University Hospital Carl Gustav Carus in Dresden, Germany. Patients were referred either by the Department of Neurology or the Department of Pediatrics for IA treatment to our unit.

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Immunoadsorption was performed using adsorber columns loaded with sheep-immunoglobulins directed against human immunoglobulins (Ig) (Therasorb-Ig™-flex, Miltenyi Biotec GmbH, Bergisch-Gladbach, Germany) and the Life18 apheresis unit (also from Miltenyi Biotec). This system contains a plasma disc separator to separate blood cells from plasma followed by 2 adsorber columns, which undergo alternating loading and regeneration cycles.

As a standard of care, we prefered to use peripheral venous access whenever possible, otherwise a double lumen central venous access was placed. Treatment efficacy was evaluated by measurement of Ig before and after individual treatment sessions. If possible, measurement of autoantibodies was also performed in serum samples or the first/second eluate from the Therasorb-Ig™ columns.

2.1. Statistics

Statistical analysis was performed using student's t-test, all data is given as mean ± standard deviation. The GraphPad Prism 5.0 software package (GraphPad Software Inc., La Jolla, CA, USA) was used.

3. Results

A total number of 16 patients was treated at our center, 8 were females and 8 were males. The mean age of patient's was 43.3 ± 23 years (range 7–79). Patients underwent an initial daily treatment for 3–4 sessions, followed by an alternating treatment regimen in the following 2 weeks until completion of 10 treatment sessions. Treatments were performed in close interaction with the Departments of Neurology or Pediatrics, where the decision for extracorporeal treatment was made and clinical assessment was done. Clinical follow up of patients was available for a mean of 9 months (range 1–456 months). As depicted in Table 1, we treated a wide spectrum of neurologic disorders including patients with multiple sclerosis and acute steroid refractory episodes, while autoantibodies could not be detected in every case. Frequently, patients have been on immunomodulatory treatment as shown in Table 2.

3.1. Treatment sessions

The mean number of treatment sessions was 8.9 (range 5–10), the mean period of the treatment (1st to last) was 14.1 days (range 7–18). In detail, 11/16 patients completed 10 sessions, one patient received 9 sessions, one patient received 8 sessions, one patient received 6 sessions and 2 patients received 5 sessions. In summary, 143 treatment cycles were performed. Despite our policy to rely on native veins whenever possible, we had to place a central venous access in most cases and only 49 sessions were performed using native veins. The reasons for this were variable: children with small peripheral veins (25×), breast feeding (10×), dependence on intensive care (29×) treatment and otherwise limited peripheral access. Except for children we aimed to treat the double calculated plasma volume. Overall, the mean blood volume treated was 15.6 L (range 9.8–23.6), the mean plasma volume treated was 7.65 L (range 3.4–7.8). The average cumulated plasma volume per patient was 53 ± 14.5 L with an interindividual range between 30 and 77.8 L.

Table 1
Overview of treated neurological indications and detectable autoantibodies.

Disease	Detectable autoantibodies
Atypical Guillain-Barre-Syndrome	No
Autoimmune cerebellitis	Yes
Multiple sclerosis with acute steroid-refractory relapse	No
Cerebellar ataxia	No
Myasthenia gravis	Yes
Autoimmune erythromelalgia	No
Progressive encephalomyelitis with rigidity and myoclonus (PERM) syndrome (unclear)	Yes
Chronic relapsing inflammatory optic neuropathy (CRION)	No
Autoimmune encephalitis	Yes
Limbic encephalitis	Yes
Neuromyelitis optica (NMO)	Yes
Chronic inflammatory demyelinating polyneuropathy (CIDP)	No
Encephalitis	No

3.2. Adverse events

Adverse events were reported in very few sessions and mainly consisted of perioral or pedal paresthesia, which related to the use of citrate anticoagulation and subsequent decrease in serum calcium levels. These side effects could easily be treated by increased application of oral or intravenous calcium. One patient repeatedly reported dysgeusia, in 1 patient a BP depression occurred and an immediate infusion of 250 mL of saline solution was necessary. Together with mild paresthesia, the overall frequency of adverse events was approximately 10%, circulatory depression had to be treated in 0.01%.

3.3. Treatment efficacy – reduction of Ig and autoantibodies

To assure treatment efficacy we measured IgG serum levels before and after each treatment and calculated IgG reduction rates. In addition, we also evaluated reduction of IgA and IgM serum levels due to Therasorb-Ig™ treatment in individual patients. Thereby, the mean IgG reduction (before versus after treatments) in all patients was −72.2 ± 8.7% (range −60.1 to −84%; $P < 0.001$), indicating a very high treatment efficacy. The mean reduction rates for IgM were −45.8 ± 11.7% (range −29 to −64; $P < 0.01$) and for IgA −56.2 ± 11.7% (range −38 to −64;