

## PLASMAPHERESIS IN NEUROLOGIC DISORDERS

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**SUMMARY** - Two decades after the initial encouraging reports on plasmapheresis in myasthenia gravis, neurologic diseases represent the most common indication for therapeutic plasma exchange. Recent studies have not only established the therapeutic importance of plasmapheresis, but have also set new standards for the management of autoimmune neurologic disorders. Plasmapheresis has proved beneficial in autoimmune neurologic diseases such as Guillain-Barre syndrome, myasthenia gravis, and paraprotein-associated polyneuropathy. In some other diseases, e.g., multiple sclerosis, polymyositis, dermatomyositis, and chronic inflammatory demyelinating polyneuropathy, plasmapheresis cannot be considered a generally accepted therapeutic option. However, in chronic autoimmune diseases such as progressive multiple sclerosis, polymyositis, dermatomyositis, and chronic inflammatory demyelinating polyneuropathy, plasmapheresis is recommended in patients whose condition continues to worsen despite immunosuppressive drug therapies, and in those for whom it is desirable to reduce the dose of corticosteroids to avoid long-term complications. Based on the initial studies, plasmapheresis in conjunction with immunosuppressive drug therapies is now standard therapy for Eaton-Lambert syndrome.

Key words: *Plasmapheresis; Autoimmune diseases of the nervous system, therapy*

### Introduction

The initial encouraging report by Dau et al.<sup>1</sup> on plasmapheresis (PP) in myasthenia gravis (MG) published more than two decades ago led to unprecedented interest in and hope for various neurologic disorders with presumed autoimmune dysfunction. Within a few years, there were many anecdotal and pilot studies to warrant controlled trials of PP in neurologic disorders such as MG, Guillain-Barre syndrome (GBS), multiple sclerosis (MS), and chronic inflammatory demyelinating polyneuropathy (CIDP). These studies have established the therapeutic importance of PP and set new standards for clinical trials in autoimmune neurologic disorders<sup>2</sup>. A pilot of an international therapeutic apheresis registry was conducted by the International Center for Artificial Organs and Transplantation for the year 1983 to collect data on PP proce-

dures and technology<sup>3</sup>. In this voluntary survey, a 24.1% response rate was received by the centers solicited. Thirty-seven centers on four continents reported data on 659 patients receiving 5,780 PP. In the East (Asia and Australia), digestive system diseases were the most commonly reported treatment diagnosis, whereas in Europe and USA neurologic disorders prevailed<sup>4</sup>.

The aim of this report is to provide an overview of the current trends and practice of PP in neurologic disorders.

### Myasthenia Gravis

Myasthenia gravis (MG) is a chronic disease that most commonly occurs in young adults and progresses with remissions and exacerbations. It is characterized by the activity-induced abnormal muscle fatigability resulting in typical drooping of eyelids and jaws, nasal voice, slurred speech, and weakness of proximal extremities. MG involves progressive failure of impulse conduction at the neuromuscular junction. It is an antibody-mediated au-

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toimmune disease in which circulating acetylcholine receptor (AChR) antibodies have been identified that bind to receptor sites in voluntary muscles, damaging and blocking the receptors<sup>5</sup>. Hyperplasia of the thymus is frequently associated, and approximately 12% of patients with MG have a thymoma.

During the early active stage of MG while the characteristic remissions and exacerbations occur and before muscle atrophy has set in, some patients may respond well to surgical removal of the thymus. Many believe that early thymectomy may decrease the level of autoimmune activity before a major permanent damage has been sustained by the AChR sites in voluntary muscles. Steroids are usually given to suppress the production of antibodies, and azathioprine was found useful in some cases<sup>2</sup>. Anticholinesterase drugs are administered to prevent the breakdown of acetylcholine at the myoneuronal junction.

The initial and ground-breaking study by Dau et al.<sup>1</sup> established the efficacy of PP in MG patients, and led to further confirmatory clinical trials<sup>6-8</sup>. The response to PP in these studies was so dramatic, that there has never been felt the need of a double-blind randomized controlled study since. In spite of this, the 1985 NIH Consensus Conference concluded that PP could be useful in increasing muscle strength during the pre- and post-thymectomy period, and in decreasing the symptoms associated with the initiation of immunosuppressive therapy and during acute crises<sup>9</sup>.

In acute myasthenic crisis, the recommended PP prescription is five sessions over a one-week period. Each session should be equal to 1.5 plasma volume (PV), which can be replaced with 5% albumin (Table 1). If the patient is in the immediate prethymectomy period, partial replacement of approximately 1 L of fresh frozen plasma (FFP), given toward the end of the last session, should help reverse the expected depletion coagulopathy<sup>10</sup>. PP therapy is then gradually decreased as tolerated by the patient. Although the levels of AChR antibodies are unlikely to be immediately available for therapy monitoring, a retrospective comparison between the observed and expected declines in AChR antibodies reveal an excellent correlation with the calculated total IgG removal kinetics<sup>11</sup>.

In patients with MG who need continued immunosuppressive drug therapy (ISDT), weekly PP therapy with gradual reduction in conventional ISDT (prednisolone, azathioprine, and cyclophosphamide) is recommended. Once the desired dosage of ISDT has been reached, the frequency of PP is gradually decreased, and patients are eventually weaned. In a small number of patients, maintenance PP therapy may become necessary for a long period of time (up to several years)<sup>2</sup>. In some patients in whom PP and conventional ISDT either cannot be decreased or the patient cannot be successfully weaned, the addition of a low dose cyclosporin (1 to 5 mg/kg body weight/day) is effective<sup>12</sup>.

*Table 1. Plasmapheresis in patients with myasthenia gravis*

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Indications

- Patients with severe motor weakness not responding to conventional therapy
- Patients with myasthenia gravis who may need surgery

Assessment of response

- Motor strength with and without physostigmine
- Acetylcholine receptor antibody titer change

Suggested therapy

- 1.5 PV sessions daily for 5 days
- Replacement of removed plasma ml/ml with 5% albumin

Precautions

- Acetylcholine receptor antibody titer does not correlate with disease severity, but relative changes do
  - Intervention in patients with chronic disease does not produce sustained improvement
  - Anticholinesterase medication given during plasmapheresis may cause cholinergic reactions consisting of bradycardia, abdominal cramping, sweating, and hypotension or respiratory arrest
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There have been no controlled studies showing the significant effect of intravenous immune globulin (IVIG), but this therapy was used with good results in some studies<sup>13,14</sup>. The ease of administration and lack of significant side effects make IVIG a good chance, either alone or in combination with PP as dictated by the disease severity<sup>2</sup>.

### Guillain-Barre Syndrome (Acute Idiopathic Polyneuritis)

Guillain-Barre syndrome (GBS), an acute, frequently postinfection (but may also occur after vaccination, injury, or surgery) polyneuritis may be due to an allergic response or some type of hypersensitivity reaction. Demyelination and degeneration of the myelin sheath and axon occur in the segmental peripheral nerves, and in the anterior and posterior spinal nerve roots. Antibodies directed against various constituents of peripheral myelin have been identified<sup>15</sup>. Inflammation, edema, and damaged nerves result in both sensory and motor dysfunction (the muscles of the trunk and upper extremities). The diagnosis is supported by the existence of an albuminocytologic dissociation in the cerebrospinal fluid<sup>16</sup>.

The treatment with steroids, ISDT, may or may not be beneficial in altering the course of the disease. The favorable outcome in earlier case reports on PP in acute GBS<sup>17-19</sup> led to three large randomized controlled trials, which for the first time firmly established an effective treatment for this disease<sup>21,22</sup>. The most compelling evidence for the efficacy of PP come from a multicenter study involving <sup>21</sup> medical centers and 245 patients with GBS, randomized to either supportive therapy or PP<sup>21</sup>. The patients receiving PP had a substantially reduced duration of muscular weakness (40 *vs.* 29 days) and required a significantly shorter period of pulmonary support (48 *vs.* 24 days)<sup>21</sup>. It should also be noted that a British randomized trial failed to conclude on the beneficial effects of PP in GBS<sup>23</sup>.

In patients with a second-grade or worse GBS (demonstrable weakness in the legs, but able to walk 5 m without a walker or equivalent support)<sup>24</sup>, PP should be initiated as early as possible. The recommended PP prescription is a total of 10 one-PV exchanges (at least 200 to 250 ml of plasma/kg body weight) delivered over a period of 14 days (Table 2). An increased frequency in the beginning of treatment, followed by PP procedure performed on alternating days is recommended<sup>25</sup>. The total

Table 2. Plasmapheresis in patients with Guillain-Barre syndrome

#### Indications

- Ascending paralysis involving upper extremities or higher level
- Decrease in pulmonary function parameters (1-min forced expiratory volume or vital capacity) to 80% of normal
- Respirator dependence
- Infusion of intravenous immunoglobulins only (without plasmapheresis) is also efficacious therapy
- However, although not statistically significant, patients randomized to plasmapheresis were started on therapy later and were sicker

#### Assessment of response

- Neurologic assessment
- Measure the forced expiratory volume at 1 min (FEV 1.0) and vital capacity every 12 hours

#### Suggested strategy

- 1-PV session daily for 5 days; then five more 1-PV sessions every other day
- Replace removed plasma with 5% albumin ml/ml during the first 3 to 4 sessions; for subsequent sessions, replace a half of the removed plasma volume with FFP instead of 5% albumin
- Continue the treatment if the patient is still respirator dependent
- Intravenous infusion of IgG (40 g) at the end of treatment may be beneficial

number of PP therapies required to improve and stabilize a GBS patient may vary from 5 to more than 15 sessions<sup>2</sup>.

A recent Dutch study compared the accepted PP regimen with IVIG, demonstrating a better or at least equal outcome with IVIG<sup>26</sup>. An accompanying review has found these results difficult to interpret because the patients treated with PP worsened more than expected<sup>15</sup>. Most recently, a comprehensive comparison of IVIG and PP for neurologic diseases has suggested that those receiving IVIG may have a tendency to relapse<sup>27</sup>.

### Chronic Progressive Multiple Sclerosis

Multiple sclerosis (MS) is a relatively common chronic and progressive inflammatory, demyelinating disease of the central nervous system that results in diverse manifestations of neurologic alteration. Its basic cause is unknown, however, it is probably an autoimmune disorder influenced by genetic susceptibility. Studies of antibodies in the blood or cerebrospinal fluid often show gammaglobulin abnormalities. The oligoclonal bands of IgG directed against the various antigens of the measles virus but no specific antigen have been isolated in multiple sclerosis<sup>28</sup>.

The treatment of multiple sclerosis is generally symptomatic, because immunosuppression using steroids, azathioprine and cyclophosphamide has provided encouraging results<sup>25,29</sup>. A larger study in which a prolonged PP protocol was used in patients taking cyclophosphamide and prednisone, showed a significant and sustained improvement in 62.2% of patients<sup>30</sup>. Clinical improvement was associated with improvement in evoked potential studies and suppressor cell functional activity in these patients. Although ISDT alone has in various studies stabilized or even brought about some improvement in MS<sup>31,32</sup>, the results of this analysis indicate that the degree of improvement and the length of disease stabilization is greater when PP is added to ISDT. An overall review of ISDT in MS leads to a conclusion that in an attempt to achieve short-term stabilization in the course of the disease, the dosage of the cytotoxic drug must be high and booster therapies are required, or therapy has to be continued for a long time<sup>2</sup>. In such a setting, the side effects of ISDT (alopecia, carcinoma) are of great concern<sup>32,33</sup>.

Results of a previous study<sup>30</sup> suggest combining ISDT with an extended use of PP not only to achieve improvement and longer stabilization of the course of the disease, but also to use a potentially less toxic short course of low dose ISDT. In 200 MS patients who received PP and such

a short course of low dose ISDT, Khatri et al.<sup>34</sup> did not record any serious side effects with the exception of one patient who manifested carcinoma of the breast 3 years after discontinuation of cyclophosphamide (this incidence is lower than the natural incidence of breast carcinoma). Even more, MS patients who received PP and ISDT showed a significant ( $p < 0.001$ ) improvement at therapy completion, and at one-, two- and three-year follow-up<sup>34</sup>. Over 80% of patients improved or stabilized at 3 years following PP and ISDT. The analysis of various clinical characteristics in those who improved after this therapy failed to show any differences according to gender, age at onset, or degree of disability at the time of treatment. Statistically significant ( $p < 0.001$ ) differences were observed in age at the time of treatment and total duration of the disease. The improvement was better in younger patients with shorter duration of MS. The degree of decline on the disability status scale (DDS) relative to the time of therapy introduction also was a significant predictor of improvement. Seventy-five percent of MS patients who improved were treated within a year from the time of their decline on DDS by one or more degrees<sup>34</sup>. The mean number of PP administered during the initial course of treatment was 24 (range, 12 to 46). Forty-three (21.5%) patients received more than one course of PP during the follow-up. These patients had initially improved and stabilized, whereafter their condition began to worsen at a variable time after the initial course of PP. A short course of PP (5 weekly sessions) restored or stabilized improvement in 81.4% of patients. Coadministration of drug therapy during retreatment consisted of prednisone (0.5 mg/kg body weight every other day) in decreasing dosages, and human IgG injections after each PP. The response to retreatment was as good as the response to the initial course. According to Khatri et al.<sup>34</sup>, it is possible to predict the outcome of MS patients treated with PP and ISDT. Table 3 presents expected improvement in DDS following PP and ISDT, while Table 4 shows chances for patient improvement by one or more degrees<sup>34</sup>.

Recently, the Canadian Multicenter Cooperative Study randomized 168 patients to cyclophosphamide and prednisone with or without weekly PP or placebo medication and sham PP<sup>35</sup>. After approximately 20 weeks of active treatment, the patients were monitored for disability scores for a mean of 30-month follow-up. In the PP group, a trend of decreasing disability was observed at 12, 18 and 24 months of the follow-up, however, the difference was not sustained at 36 months<sup>35</sup>.

Table 3. Expected change on disability status scale in patients with chronic progressive multiple sclerosis following plasmapheresis and immunosuppressive drug therapies<sup>35</sup>

Patient age (yrs)	Worse by $\geq 1$ DSS in previous year			Worse by $< 1$ DSS in previous year		
	Duration of multiple sclerosis (yrs)					
	<3	3-7	>7	<3	3-7	>7
<33	3.9	1.7	1.5	2.2	0.6	0.1
33-40	1.9	0.8	1.2	1.1	0.6	0.2
>40	1.2	2.5	1.0	0.8	0.5	0.4
	Bootstrap standard errors					
<33	0.7	0.4	0.8	0.8	0.3	0.1
33-40	0.6	0.2	0.3	0.5	0.2	0.1
>40	0.6	0.4	0.2	0.5	0.2	0.1

Table 4. Chance for one or more step improvement on disability status scale in patients with chronic progressive multiple sclerosis following plasmapheresis and immunosuppressive drug therapies<sup>35</sup>

Patient age (yrs)	Worse by $\geq 1$ DSS in previous year			Worse by $< 1$ DSS in previous year		
	Duration of multiple sclerosis (yrs)					
	<3	3-7	>7	<3	3-7	>7
	%	%	%	%	%	%
<33	95	86	68	76	36	26
33-40	66	77	63	56	76	20
>40	77	95	77	55	54	39
	Bootstrap standard errors					
<33	5	14	30	16	19	17
33-40	15	24	12	20	16	13
>40	23	5	12	17	14	7

In a pilot study, PP along with recombinant alpha interferon produced a significant improvement in 21 of 24 patients with progressive MS<sup>36</sup>.

The exact mechanism of PP action in progressive MS is not known. According to one hypothesis, the improvement in the functional activity of suppressor T cells following PP is associated with clinical improvement in progressive MS<sup>31</sup>. Another hypothesized mechanism involves removal of circulating toxins, antigens, or antibodies that acutely damage myelin sheaths or oligodendrocytes<sup>37</sup>. The removal of the interferon inhibiting factor by PP therapy can result in increased circulating interferon alpha concentrations, and a significant clinical improvement<sup>38</sup>.

At present, PP cannot be considered a generally accepted therapeutic option for MS<sup>2,25</sup>. The Writing Committee of the American Society for Apheresis recommends the use of PP in chronic progressive MS when conventional therapy has failed to either stop the progression of the disease, or to improve patient condition as well as when conventional therapy is contraindicated<sup>39</sup>. The recommended protocol is one PV PP *per* week for 10 weeks in conjunction with prednisone (1 mg/kg body weight every other day) and cyclophosphamide (1 mg/kg body weight/day). If the patient shows objective improvement, PP and ISDT are tapered over time until patient stabilization is achieved (mean, up to 20 PP sessions). A

small group of MS patients may need maintenance therapy once every 6 to 10 weeks, with or without prednisone<sup>39</sup>. PP therapy is discontinued if no objective improvement is observed at the end of 10-week treatment.

### Chronic Inflammatory Demyelinating Polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (CIDP) is believed to be an autoimmune disease, and is characterized by a progressive or relapsing course, symmetrical motor or motor and sensory loss, hyporeflexia or areflexia, and absence of systemic symptoms. Humoral and cellular immune dysfunctions have been implicated in the pathogenesis of CIDP<sup>40</sup>. Abnormalities supporting the diagnosis include elevated cerebrospinal fluid protein, severe slowing of nerve conduction velocity, and segmental demyelination on nerve biopsy. The condition can progress to severe disability or death<sup>41</sup>.

A potential benefit from plasma exchange therapy has previously been reported from several uncontrolled studies<sup>4</sup>. The most convincing data come from a randomized, sham-controlled trial in severely affected patients<sup>40</sup>. Treatment prescription included 2 PV exchange procedures *per* week for 3 weeks. Each plasma exchange averaged 1 to 1.5 PV, and replacement fluid was 5% albumin. Approximately 30% of those treated with PP responded with improved DDS and nerve conduction. There was no prospective means of identifying the responders. In those patients who responded, improvement generally began to fade within 10 to 14 days after the treatment discontinuation, suggesting that a maintenance treatment schedule may be required to sustain remission. This study firmly established the usefulness of PP in CIDP<sup>41</sup>. While ISDT has been recommended in CIDP, in those patients who do not respond adequately or need long-term ISDT, PP should be considered. As CIDP is a chronic disease, PP needs to be combined with ISDT. The dosages and duration of ISDT are much lower when therapies are used in combination with PP<sup>41</sup>. A recent report has established the need of long-term treatment of CIDP with PP<sup>43</sup>. Indeed, a preliminary report by Feasby et al.<sup>44</sup> shows that maintenance of neurologic improvement required PP to be performed at a schedule ranging from weekly to every 3 weeks for up to 60 months.

Khatri and Wroblewski<sup>45</sup> have reported on a retrospective study in 31 patients with CIDP resistant to conventional therapy, who were treated with PP. In most of

these patients, PP produced significant improvement, however, 11 (35.5%) patients required continued PP therapy (mean, 3.6 years). A majority of the remaining 20 (64.5%) patients who were successfully weaned from PP, required at least 12-month treatment<sup>45</sup>.

Dyck et al.<sup>46</sup> randomized and treated 20 CIDP patients with either PP or IVIG for 6 weeks, followed by washout period, and then switched to another treatment. The PP treatment protocol included 2 PP sessions a week for 3 weeks, then once a week for the next 3 weeks. According to the IVIG protocol, CIDP patients received immune globulin (0.4 g/kg body weight) once a week for 3 weeks, then 0.2 g/kg body weight once a week for the next 3 weeks. In both the PP and IVIG treated group of CIDP patients, a statistically significant improvement occurred in DDS and summation compound muscle action potentials ( $p < 0.001$ )<sup>46</sup>. In another open study in 67 consecutive CIDP patients, the response rates were similar in the ISDT, IVIG and PP treated patients, whereas functional improvement was greatest in the group of patients treated with PP<sup>47</sup>.

In CIDP patients, the PP therapeutic protocol is individually tailored according to the disease severity. Most patients are initially treated with ISDT, and PP is only initiated when there is no response to previous therapy, or if it appears that the patient may need a high dosage long-term steroid therapy. Minors receive PP twice a week for 3 weeks, then once a week for 3 weeks. If objective improvement is noted, PP is continued to be tapered until the patient can be safely weaned from treatment<sup>2</sup>. In patients without objective improvement after the initial 9 PP sessions as well as in those who cannot be weaned from PP, the addition of ISDT or IVIG should be considered. Patients with a severe form of CIDP may need to be treated with maintenance long-term PP with or without ISDT or IVIG therapy<sup>2</sup>.

### Paraprotein-associated Polyneuropathy

The presence of monoclonal antibodies (IgM, IgA, and IgG) may be associated with antibody binding to certain constituents of peripheral myelin and consequential neuropathy. Cellular immune dysfunction has also been implicated in the pathogenesis of this syndrome. A demyelinating process is characterized by distal weakness, tremor, ataxia and loss of perception<sup>30</sup>. The cancer usually remains localized, but the patients die from neurologic dysfunction.

Removal of these immunoglobulins is the rationale for PP therapy. In a randomized, sham-controlled trial in patients with paraprotein-associated polyneuropathy, Dyck et al.<sup>48</sup> found that sensorimotor neuropathy improved significantly in patients receiving PP. The treatment prescription was 2 PP weekly for 3 weeks. Each plasma exchange averaged 3.5 L, and replacement fluid was 5% albumin<sup>48</sup>. Further investigation is warranted to determine the role of aggressive PP in conjunction with ISDT in paraprotein-associated polyneuropathy.

### Eaton-Lambert Syndrome

Eaton-Lambert syndrome (ELS) is a myasthenia-like syndrome, clinically manifested with proximal muscle weakness, easy fatigability, and autonomic dysfunction. It may be cancer-related or idiopathic. Pathophysiologically, it is the result of antibody-mediated blockage of acetylcholine release by the presynaptic nerve terminal, causing disruption of calcium channels, which in turn leads to a decreased calcium flux across the membrane. The humoral and cellular immune dysfunction has been implicated in the pathogenesis of ELS, and in 70% of patients the disease is associated with cancer (usually an oat cell carcinoma of the lung)<sup>49</sup>.

Dau and Denys<sup>50</sup> describe clinical and electromyographic improvement in patients treated with PP. The underlying tumor must also be treated.

Based on the initial studies<sup>50,51</sup>, PP should be carried out twice weekly for 3 weeks, then weekly for 3 weeks, followed by a gradual weaning process. PP therapy is usually combined with ISDT (azathioprine 1-2 mg/kg body weight/day, and prednisolone in a dose of 1 mg/kg body weight/day) in a declining fashion<sup>2</sup>.

### Polymyositis and Dermatomyositis

Polymyositis (PM) and dermatomyositis (DM) are inflammatory muscular diseases of unknown etiology. In the pathogenesis of these diseases, both humoral and cellular immune dysfunction is implicated<sup>52</sup>.

Patients with PM and DM are classically treated with steroids. In patients resistant to steroids or in whom their side effects are unacceptable, other immunosuppressive agents (cyclophosphamide, cyclosporin), IVIG, total body irradiation, and PP have been used<sup>53</sup>. Dau<sup>54</sup> was the first to report on the efficacy of PP in steroid resistant PM and

DM, while in a recent multicenter study of PP in 57 patients with PM and DM<sup>55</sup> the most significant improvement was observed in patients with acute inflammatory myopathies (but not in subacute or chronic patients).

PP is recommended in PM and DM patients whose condition continues to worsen in spite of steroid therapy, and in those who need high steroid doses (to avoid long-term steroid complications). The PP protocol is twice weekly for 3 weeks, then weekly for 3 weeks, followed by a gradual weaning process. Coadministration of ISDT is important, and consists of low doses of cyclophosphamide, azathioprine, methotrexate, and prednisolone.

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## Sažetak

## PLAZMAFEREZA U NEUROLOŠKIM BOLESTIMA

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Dva desetljeća nakon početnih ohrabrujućih rezultata liječenja miastenije gravis pomoću plazmafereze, neurološke bolesti danas su najčešća indikacija za terapijsku izmjenu plazme. Plazmafereza je korisna metoda u liječenju autoimunih neuroloških bolesti poput Guillain-Barreova sindroma, miastenije gravis i polineuropatije uzrokovane paraproteinima. U nekim drugim neurološkim bolestima (multipla skleroza, polimiozitis, dermatomiozitis, kronična upalna demijelinizirajuća polineuropatija) plazmafereza nije općenito prihvaćeni način liječenja. Međutim, u kroničnim autoimunim bolestima kao što su multipla skleroza, polimiozitis, dermatomiozitis i kronična upalna demijelinizirajuća polineuropatija, plazmafereza se preporuča u bolesnika u kojih nije došlo do poboljšanja usprkos terapiji imunosupresivnim lijekovima, te u onih bolesnika u kojih je potrebno smanjiti dozu kortikosteroida kako bi se izbjegle komplikacije koje mogu nastati zbog dugotrajne terapije. Plazmafereza i imunosupresivni lijekovi danas su standardna terapija za Eaton-Lambertov sindrom.

*Ključne riječi: Plazmafereza; Autoimune bolesti živčanog sustava, terapija*