

Mellen Center Approaches: Plasmapheresis in MS

What is plasmapheresis?

Plasmapheresis (also known as apheresis, plasma exchange, or “plex”) is a medical procedure where a device separates whole blood into the cellular components and plasma. The plasma is then discarded and replaced with a colloid fluid, combined back with the cellular components, and returned to the same patient. The colloid fluid is typically a combination of human serum albumin and/or fresh frozen plasma. Typically, a large-bore, double-lumen catheter is used to provide sufficient volume of blood to perform plasmapheresis over several hours.

Where is plasmapheresis used in MS and related disorders?

Plasmapheresis is used as a second-line therapy (after systemic corticosteroids) in the management of multiple sclerosis (MS) relapses (or “attacks”) and other central nervous system (CNS) demyelinating diseases including acute disseminated encephalomyelitis, idiopathic transverse myelitis, idiopathic optic neuritis, and neuromyelitis optica. Plasmapheresis is occasionally used inpatients who are intolerant of high-dose corticosteroids or who have medical contraindications to high-dose corticosteroids.

Are there clinical trials showing efficacy of plasmapheresis?

Two controlled trials evaluated the effect of plasmapheresis. One study of 116 MS patients in an acute exacerbation randomized patients to 11 courses of plasmapheresis or sham treatment over eight weeks.¹ This treatment was added to oral cyclophosphamide and adrenocorticotrophic hormone (ACTH). There was no overall difference between the two groups, although there was a trend at one month in favor of plasmapheresis. A second randomized, sham-controlled trial evaluated 22 patients with severe deficits from a variety of CNS inflammatory disorders who had been refractory to high-dose corticosteroids.² Those

randomized to plasmapheresis were more likely to improve, and the improvement was sustained after treatments stopped.

How many exchanges are performed?

There is no set number of plasma exchanges performed, although typically patients receive between three and seven exchanges, each of which take 2-4 hours. The number of treatments can be guided by the clinical recovery, or sometimes a preset number of exchanges are performed. For management of natalizumab-related progressive multifocal leukoencephalopathy, five exchanges are recommended.

What types of patients are more likely to improve following plasmapheresis?

A retrospective study found that 44% of patients treated with plasmapheresis had a moderate or marked improvement.³ Improvement was more likely in patient with neuromyelitis optica (NMO) and Marburg variant MS. In addition, improvement was seen more commonly in men, those with preserved reflexes, and when treatment was started within 20 days of onset. Another study confirmed many of these observations.⁴ At the Mellen Center, we consider plasmapheresis in patients who with less than 1-2 months of severe neurologic impairment secondary to CNS demyelination or inflammation.

Is plasmapheresis used in neuromyelitis optica (NMO) and acute disseminated encephalomyelitis (ADEM)?

NMO is a rare (~1% the incidence of typical MS) inflammatory disease manifest as longitudinally extensive transverse myelitis, optic neuritis, and occasionally atypical brain lesions. A highly specific auto-antibody to the aquaporin-4 water ion channel is seen in the majority of patients with NMO

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syndrome. High-dose corticosteroids are the typical first-line treatment for acute attacks of NMO, but corticosteroids are often insufficiently effective in NMO. Given the probable pathogenic role of anti-aquaporin-4 antibodies in serum, it is not surprising that plasmapheresis has been reported to be effective in NMO.³⁻⁵ Repeated courses of plasmapheresis have also been reported to be effective in patients who did not respond to oral immunosuppressive therapies alone.⁶ Case series report improvement following plasmapheresis in patients with ADEM, too.^{7,8}

Is plasmapheresis effective in progressive MS?

Several trials have evaluated plasmapheresis in progressive MS. A meta-analysis of six trials found modest evidence for reducing the odds of worsening over 12-36 months. However, the control groups were not all comparable and other immunosuppressive treatment were administered, making it difficult to assess the efficacy of plasmapheresis. Given marginal data on efficacy, the logistical challenges of administering plasmapheresis, and the cost of plasmapheresis, we do not generally recommend plasmapheresis in the treatment of progressive MS.

How is plasmapheresis used in the management of progressive multifocal leukoencephalopathy (PML)?

When PML is associated with treatment with a monoclonal antibody (i.e. natalizumab), plasmapheresis is typically recommended to accelerate the removal of the therapeutic antibody with the goal of accelerating immune reconstitution. This immune reconstitution is thought to help the immune system fight the CNS infection which causes PML. In the setting of natalizumab therapy, plasmapheresis has been found to accelerate the removal of natalizumab, accelerate desaturation of the α 4-integrin receptors, and improve leukocyte transmigration across an in vitro blood brain barrier.⁹ However, it remains unclear if this treatment improves the ultimate outcome of PML in this setting.

What is required to perform plasmapheresis?

Plasmapheresis is a specialized medical procedure, typically performed in a dedicated plasmapheresis unit. It requires large-bore intravenous catheters to provide sufficient rate of blood flow through the machine. At our institution, Quinton catheters are typically used and have provided reliable intravenous access and excellent safety. Large-bore catheters are typically placed by Interventional Radiology. Outpatient treatment is possible, although most patients who need plasmapheresis for CNS demyelination are hospitalized because of the complications of their underlying condition. Because there are few randomized trials of plasmapheresis, insurance coverage of the procedure is sometimes difficult.

What are the risks of plasmapheresis?

Several reactions may occur during plasma exchange, including fainting, dizziness, or nausea, all of which are caused by hypotension. To reduce the risk of hypotension, patients should be encouraged to drink 6-8 glasses of non-caffeinated fluids each day starting three days before the first treatment. Rarely, patients report paresthesias because of a reaction to the blood thinner, which is treated with extra calcium. Fatigue is sometimes reported by patients after plasma exchange, but typically goes away the next day. Other risks include bleeding or an allergic reaction (itching, wheezing, or rash) to the solutions used to replace the plasma or the sterilizing agents used for the tubing.

Excessive suppression of the immune system can temporarily occur due to plasma exchange, which can increase the risk of infection. Rarely, the blood may clot in the machine, making return to the patient impossible. Very rarely, deaths have been reported with plasma exchange, usually from infection or the underlying condition for which plasma exchange treatment was used.

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