CORRESPONDENCE

Therapeutic Plasma Exchange in Patients with Neurologic Disorders: Insufficient Evidence to Support the Use of Hydroxyethyl Starch

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Dear editor,

A recent article by Tombak et al. [1] investigated the use of therapeutic plasma exchange (TPE) with either albumin or hydroxyethyl starch (HES) in a small cohort of 63 patients with mixed neurological disorders. This retrospective study confirmed that TPE is an effective treatment in certain neurologic diseases. In addition, the authors advocate the use of HES over albumin as the replacement fluid of choice, citing similar efficacy and complication rates combined with an improved cost profile as the reasoning. However, the study has several limitations which raise questions regarding the validity of these findings.

The study design is primarily limited by its observational retrospective nature; all data is non-randomised, non-blinded and reliant on availability and accuracy of medical records. Furthermore, important data are not reported; for example, details relating to TPE frequency, medical history and clinical decision-making are not included. The data on patient follow-up is limited; adverse events during the procedure were captured; however, no assessment of long-term outcomes, such as mortality and kidney function,

were undertaken. Additionally, the small sample size in each treatment group (31 patients on both albumin and HES) restricts the validity of these results. Patients spanned 10 different neurologic disorders and could not be stratified by disorder. Therefore, no conclusions can confidently be drawn regarding the use of HES in any of these conditions.

In addition to the study limitations, the results from Tombak et al. contradict a number of earlier studies and are also not in-line with current guidance on the use of HES products. The use of TPE has seen a 10% decrease in the number performed for neurological conditions already between 1988 and 2003 [2]. This decline reflects the growing use of evidence-based practice and advantages in alternative treatments that replace TPE in certain conditions. Currently, TPE is still indicated in some neurologic disorders; however, evidence suggests it may be ineffective or harmful for several of the conditions treated in this study, such as multifocal motor neuropathy (MMN) and polymyositis (Table 1) [3]. An observational study of seven MMN patients found that all patients had worsened electrophysiology parameters following TPE, and two experienced some deterioration in function (ref. in [3]). Furthermore, in the study by Tombak et al. some patients received intravenous immunoglobulin (IVIG) treatment prior to TPE. This is despite previous studies showing a limited therapeutic benefit of TPE in patients who previously received IVIG treatment [3]. Therefore, it should be questioned why these patients were treated with TPE in this study.

Finally, following concerns in 2013, the Food and Drug Administration (FDA) and European Medicines Agency (EMA) decided that HES should no longer be used in critically ill patients, including those with sepsis (<https://www.fda.gov/safety/medwatch>). This action prompted the American Society for Apheresis (AFSA) to remind

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Table 1 Evidence-based indication of TPE for nervous system diseases [3]

Indication	Category	Evidence
Guillain-Barré syndrome (GBS)—primary treatment	I	1A
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)		1B
Myasthenia gravis—moderate to severe		1B
Paraproteinemic demyelinating neuropathies/chronic acquired demyelinating polyneuropathies—IgA, IgG		1B
Encephalitis associated with <i>N</i> -methyl D-aspartate receptor antibodies		1C
Myasthenia gravis—pre-thymectomy		1C
Paraproteinemic demyelinating neuropathies/chronic acquired demyelinating polyneuropathies—IgM		1C
Progressive multifocal leukoencephalopathy associated with natalizumab		1C
Multiple sclerosis—acute central nervous system inflammatory demyelinating disease	II	1B
Neuromyelitis optica (NMO) spectrum disorders—acute		1B
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) exacerbation		1B
Acute disseminated encephalomyelitis (ADEM): Steroid refractory		2C
Hashimoto's encephalopathy: steroid-responsive encephalopathy associated with autoimmune thyroiditis		2C
Lambert-Eaton myasthenic syndrome		2C
Paraproteinemic demyelinating neuropathies/chronic acquired demyelinating polyneuropathies—anti-MAG neuropathy	III	1C
Multiple sclerosis—Chronic progressive		2B
Sydenham chorea, severe		2B
GBS—after intravenous immune globulin		2C
Chronic focal encephalitis (Rasmussen encephalitis)		2C
Complex regional pain syndrome, chronic		2C
Neuromyelitis optica (NMO) spectrum disorders—Maintenance		2C
Paraneoplastic neurologic syndromes		2C
Sensorineural hearing loss, sudden		2C
Stiff-person syndrome		2C
Thrombotic microangiopathy—shiga toxin-mediated, with severe neurologic symptoms	IV	2C
Multifocal motor neuropathy (MMN)		1C

Category I: Disorders where apheresis is accepted as first-line therapy, either as a standalone treatment or in conjunction with other therapies

Category II: Disorders where apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other therapies

Category III: Disorders for which the optimum role of apheresis therapy is not established

Category IV: Disorders for which published evidence demonstrates or suggests apheresis to be ineffective or harmful

Evidence: Grade 1: Strong recommendation; Grade 2: Weak recommendation

Evidence quality: A—High-quality; B—Moderate-quality; C—Low/Very low-quality

practitioners of the risks with HES in volume replacement; including mortality and kidney failure (for review see [4]). Where TPE is appropriate, albumin is safe and albumin or albumin/saline combinations are most commonly used as the replacement fluid [3]. HES is not recommended due to its potential side effects. The frequency and types of complications from therapeutic apheresis depends upon the number of procedures and the replacement fluid [3, 5]. In many neurological indications, TPE needs to be repeated several times before being effective. This may increase the risk of HES associated adverse events particularly as HES side effects have been shown to be long lasting because it may accumulate in tissue when used in accumulating doses [6–8].

In conclusion, we cannot agree with Tombak and colleagues that HES should be used instead of albumin in neurology patients undergoing TPE due to a lack of supporting evidence and numerous study limitations. Furthermore, given the associated safety concerns with HES, albumin should remain the recommended replacement fluid for TPE in neurological disorders [2, 3].

Compliance with Ethical Standards

Conflict of interest CJW has received fees for speaking and travel cost reimbursements from CSL Behring, Grifols, Baxter and Kedrion. AP and GG have no conflict of interest to declare.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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