Management of Thrombotic Microangiopathic Hemolytic Anemias with Therapeutic Plasma Exchange

When It Works and When It Does Not

Tahir Mehmood, MD[a], Michelle Taylor, MD[b], Jeffrey L. Winters, MD[c,*]

KEYWORDS

• Plasma exchange • Plasmapheresis • Thrombotic microangiopathy
• Thrombotic thrombocytopenic purpura • Hemolytic uremic syndrome • Apheresis

KEY POINTS

- Thrombotic microangiopathies (TMA) are inherited and acquired disorders characterized by microangiopathic hemolytic anemia, thrombocytopenia, and organ damage resulting from microvasculature occlusion.
- Randomized controlled trials involving plasma exchange (TPE) exist only for thrombotic thrombocytopenic purpura (TTP) with evidence supporting use in other TMA consisting of low- to very low-quality evidence.
- The American Society for Apheresis considers TPE ineffective for the treatment of Shiga toxin–mediated TMA, selected complement-mediated TMA, and selected drug-associated TMA.
- The usual course of TPE applied to TTP is usually applied to the other TMA.
- The usual replacement fluid used in TMA is plasma, with the exception of *Streptococcus pneumoniae*-associated hemolytic uremic syndrome, where albumin is the suggested replacement fluid.

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[a] Division of Hospital Internal Medicine, Department of Internal Medicine, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905, USA; [b] Transfuse Solutions, Inc, 413 9th Avenue Northwest, Byron, MN 55920, USA; [c] Division of Transfusion Medicine, Department of Laboratory Medicine and Pathology, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905, USA
* Corresponding author.
E-mail address: winters.jeffrey@mayo.edu

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INTRODUCTION

Thrombotic microangiopathies (TMA) are a heterogeneous group of disorders, some inherited and some acquired, that share common clinical features. These features are microangiopathic hemolytic anemia (MAHA) (**Box 1**), thrombocytopenia, and organ damage due to microvasculature endothelial damage.[1] Although several disorders are considered to be TMA, this review is limited to those for which the use of plasma exchange (TPE) has been described in the medical literature. The disorders discussed are briefly described in **Table 1**. Of note, in addition to the traditional names used, **Table 1** also provides alternate names, where available, in parentheses as recommended by George and Nester.[1] These suggested alternate names are intended to provide clarity when discussing these disorders by describing the cause of the TMA.[1]

TPE is a medical procedure whereby plasma is removed and replaced with a colloid or a combination of a colloid and crystalloid replacement fluid.[2] The potential mechanisms of actions of TPE are numerous and vary according to the disease entity being considered.[3] In the case of the TMA, possible mechanisms of action include the removal of pathologic antibodies, the removal of abnormal plasma proteins, and the replacement of absent or abnormal plasma proteins.[3] The American Society for Apheresis (ASFA) provides guidance on the use of TPE in the treatment of many, but not all, of the TMA.[2] The role of apheresis therapy in the treatment of a disorder is defined by the ASFA category, with the ASFA recommendation grade providing an indication of the strength of the recommendation to perform the procedure and the quality of the published evidence supporting the treatment. These ASFA categories and the ASFA recommendation grade are defined in **Box 2** and **Table 2**, respectively, and given for each disorder, where available, in **Table 1**. Key considerations in using TPE to treat any disorder are listed in **Box 3** and are again described for many of the TMA in the ASFA guidelines. This information is provided in the sections discussing the various TMA.

THROMBOTIC THROMBOCYTOPENIC PURPURA (ADAMTS13 DEFICIENCY-MEDIATED THROMBOTIC MICROANGIOPATHIES)

Thrombotic thrombocytopenic purpura (TTP) is a rare disorder that carries a high risk of mortality if prompt treatment is not initiated. ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) is a proteolytic enzyme that cleaves ultra-large von Willebrand factor multimers (UvWF) into smaller monomers. Congenital absence of ADAMTS13 or presence of an inhibitor leading to decreased activity level has been established as the underlying pathophysiology of TTP. UvWF circulate in the plasma and bind platelets leading to microthrombi in small blood vessels, resulting in clinical manifestations of TTP including MAHA,

Box 1
Features of microangiopathic hemolytic anemia

- Anemia
- Schistocytes
- Decreased haptoglobin
- Elevated LDH