The Scleroderma Education Project™

Therapeutic Plasma Exchange Series

Therapeutic Plasma Exchange for the Treatment of Systemic Sclerosis

An Overview for Clinicians

Background

From the American College of Rheumatology Position Statement on FDA Labels*:

> "Systemic sclerosis affects approximately 75,000 to 100,000 people in the U.S. and has the single highest mortality rate of any autoimmune rheumatic disease. In spite of the grave threat posed by this diagnosis, there is no FDA-approved therapy for systemic sclerosis. Thus, rheumatologists and other providers routinely and appropriately recommend the off-label use of a range of therapies including cyclophosphamide, mycophenolate mofetil, and methotrexate."

Therapeutic plasma exchange (TPE) is a widely used treatment for a number of diseases such as myasthenia gravis, Guillain-Barre, hyperviscosity syndromes, and monoclonal gammopathy of unknown significance (MGUS). The use of TPE is not regulated by the FDA. The American Society for Apheresis (ASFA) publishes evidence based guidelines for the use of TPE for various diseases. Currently, ASFA classifies TPE for treating systemic sclerosis as a Category III treatment: "Optimum role of apheresis therapy is not established. Decision making should be individualized."

TPE has been used as a treatment approach for systemic sclerosis (SSc) since 1978 based on the rationale that some circulating factor is involved in disease pathogenesis, e.g., autoantibodies or immune complexes, and, that removing the potential pathogenic factors could lead to disease improvement. A comprehensive review of almost all of the published research on the use of TPE as a treatment was recently published in the *Journal of Scleroderma and Related Disorders*. Here is a summary of the findings from that review:

- The 46 reviewed articles totaled 572 patients, of which 455 received TPE. Nineteen of the articles were case reports involving a total of 26 patients. The remaining articles included randomized controlled trials, quasi-experimental studies, observational

* American College of Rheumatology Position Statement. FDA Labels. https://www.rheumatology.org/Portals/0/Files/Position-Statement-FDA-Labeling.pdf.

studies, and single-group pre-post studies. Quality of evidence ratings are included for all reviewed articles.

- In 25 of the 46 reviewed articles, TPE was the sole systemic intervention. In the rest of the cases, TPE was combined with additional systemic treatments, typically immunosuppressants such as mycophenolate mofetil or cyclophosphamide.
- In almost all studies, the majority of patients receiving TPE showed improvements in both symptoms and laboratory markers, whether in short-term treatment for crisis situations or from long-term administration of regular TPE.
- Many patients experienced significant improvement in Raynaud's symptoms and demonstrated early initial healing of digital ulceration after just three to four weekly treatments.
- While the effects of even a few TPE treatments often lasted for several months, only continued long-term treatments resulted in stabilization of symptoms or, in one recent case report, sustained remission over a 22-year period.
- Venous access problems occurred in a minority of patients receiving long-term TPE, leading to cessation of TPE treatments in six patients, and switching to central venous access in about 12 patients.
- TPE was extremely well tolerated by virtually all patients. Adverse events were rare and, in almost all cases, mild, with no reported deaths.

The review concludes that:

> "… in contrast to current immunosuppressive treatments that carry significant risk, long-term TPE appears to be safe, well-tolerated, and associated with only very few, mostly minor side effects. While TPE is not an inexpensive procedure, annual costs are similar to modern pharmaceuticals commonly used to treat SSc and other autoimmune diseases."

and stresses the need for a well-designed clinical trial using modern TPE equipment and improved venous access techniques.

Additional Resources

If you are considering trying TPE as an intervention for any of your patients, here are four resources that you may find helpful:

- Video: "Therapeutic Plasma Exchange for the Treatment of Systemic: A Guide for Clinicians". This video presentation about TPE is a comprehensive overview on TPE for clinicians. It summarizes the information in the published review and includes topics of interest to clinicians such as safety, cost, and insurance coverage.

  Link: sclerodermainfo.org/link/TPE-Video

- "Therapeutic Plasma Exchange for the Treatment of Systemic Sclerosis: A Comprehensive Review and Analysis". This is the comprehensive review published in the Journal of Scleroderma and Related Disorders.

  Link to publisher's website (Open Access): sclerodermainfo.org/link/TPE-Review.

- "Successful Long-Term (22 Year) Treatment of Limited Scleroderma Using Therapeutic Plasma Exchange: Is Blood Rheology the Key?". This case report, published in Clinical Hemorheology and Microcirculation, documents the effects of very long term TPE as the sole systemic intervention in a patient with diagnosed limited cutaneous systemic sclerosis (CREST).

  Link (US Format): sclerodermainfo.org/link/TPE-Case-Report-US
  Link (A4 Format): sclerodermainfo.org/link/TPE-Case-Report-A4

- "Suggested Protocol for a One-Year Trial of Therapeutic Plasma Exchange for Treating Systemic Sclerosis". This document gives a starting point for clinicians to use if they decide to move forward with a TPE trial. It also includes suggested subjective and objective measures that can be helpful in monitoring treatment effectiveness.

  Link (US Format): sclerodermainfo.org/link/TPE-Guidelines-US
  Link (A4 Format): sclerodermainfo.org/link/TPE-Guidelines-A4

- "Therapeutic Plasma Exchange: A Guide for Newbies". This is a document for patients who are about to start TPE and gives suggestions on how to make the TPE treatment experience as successful and comfortable as possible.

  Link (US Format): sclerodermainfo.org/link/TPE-Newbies-US
  Link (A4 Format): sclerodermainfo.org/link/TPE-Newbies-A4

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