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Unlocking the Potential of Blood

A UNIVERSITY HOSPITAL'S SOLUTION TO RISING COSTS OF TREATMENTS FOR NEUROMUSCULAR DISEASES

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The worldwide demand for intravenous immunoglobulin (IVIg) has doubled each decade since 2000, much of it due to a surge in the use of IVIg for the treatment of neuromuscular and neuropathic diseases.[3] Therapeutic plasma exchange (TPE), also known as plasmapheresis, has been reported as an equally efficacious treatment for certain indications, as demonstrated in published controlled trials. In our experience in 1997, a course of IVIg and an equivalent course of TPE were equal in cost. However, because it was viewed as more convenient for the prescriber, neurologists preferred IVIg.

By 2007, the price of IVIg in the U.S. had more than doubled, from $26 per gram in 1997 to $57 in 2007.[2] Due to the increased plasma volume demand and a need for improvement in production yields and collections worldwide, the supply could not meet demand. Therefore, IVIg treatments may have been denied or delayed. At about the same time, the United Kingdom's National Health Service (NHS) confronted the same issue and published a list of disease indications where TPE should be used instead of IVIg.[3]

To respond to both the unmet need and rising costs, the hospital pharmacy at UCSD started an urgent initiative to find ways to control the utilization of IVIg and manage the impact of increasing costs. UCSD's detailed analysis of costs showed that a course of **five standard infusions of IVIg was more than twice as expensive as five TPE treatments**. The analysis accounted for the full costs of TPE, including central venous access placement, amortization of the TPE machine, apheresis nurse time and supplies, as compared with costs of IVIg treatments. Subsequently, a similar study at Mayo Clinic was published, indicating that in Guillain-Barré syndrome (GBS) patients, "... direct costs of IVIg therapy are more than twice that of TPE.[4] Given equivalent efficacy and similar severity and frequencies of adverse events, TPE appears to be a less expensive first-line therapy option for treatment of patients with GBS."[4]

> **Collaboration among neurology, apheresis and pharmacy was essential to driving change.**

In 2008, UCSD introduced a plan aimed at reducing the overutilization of IVIg by using TPE instead of IVIg in suitable cases. In preparation, several meetings were held with the UCSD Neurology Department MDs. Involving them in the design phase made them stakeholders and advocates for the use of TPE. The plan had multiple elements. On the inpatient side, after approval by all stakeholders and institutional review, the computer order entry system was modified so that selecting IVIg for key neurological diseases for which TPE is an alternative treatment required pre-approval. When IVIg was selected, a prompt asked for the diagnosis for which IVIg was being requested; when certain diagnoses were checked, a second screen came up that stated "Note: Plasma Exchange is the preferred treatment for this condition, being equally effective and substantially less costly." The system then provided instructions on how to access the TPE service and required faculty-level approval to override if IVIg was still selected as the treatment option.

This effort resulted in a **marked increase in the number of inpatients receiving TPE** for various neurological conditions and, conversely, it resulted in financial savings associated with a decrease in IVIg usage. Arranging TPE treatment was convenient for the neurologist because the apheresis physician took care of writing detailed orders, assessing the type of vascular access required and managing the TPE treatments. Patients at UCSD had fewer adverse reactions to TPE than to IVIg. In addition, from our experience, the time to discharge a patient did not change, and subsequent outpatient TPE was equally as available as outpatient IVIg infusions.

During this time there was an **increase in the number of outpatients converting from chronic IVIg regimens to TPE treatments**. This increase is likely a reflection of physician awareness of the inpatient experience of TPE as a viable alternative. The increase in TPE treatments was also encouraged by a planned series of outreach seminars by the apheresis director to various groups of community neurologists. This outreach resulted in educating neurologists on TPE including accessibility, time requirements and safety of the treatments.

In our experience, patients who had suffered headaches with IVIg infusions or who were having diminishing responsiveness to treatment were vocal about their improved experience on outpatient TPE.

As word spread, increasing numbers of neurology patients were referred for initial treatment with outpatient TPE, both new cases and those converting from IVIg. A change in practice patterns favoring TPE has persisted in the region, although it appears necessary to repeat outreach seminars periodically to spread awareness to new neurologists who come to the San Diego area. The volume of TPE procedures at UCSD Medical Center has grown from about 100 cases monthly to our current volume of over 400 procedures each month in 2016.

The risk of acute kidney failure as a side effect of IVIg has diminished with improved formulations, but headaches and occasional frank aseptic meningitis remain of concern.[5]

Today, a shortage of IVIg does not exist; however, it is something to keep in mind as the demand for IVIg continues to increase. The average selling price (ASP) of immunoglobulin is about $76 per gram in 2016, almost three times what it was in 1997, while the cost of TPE supplies has only modestly changed.[1] A collaborative approach among pharmacy, neurology and apheresis helped drive efforts to manage IVIg utilization and minimize costs by using plasma exchange as an alternative therapy. In addition, given current healthcare trends and financial constraints, along with the focus on delivering quality, cost-effective care, TPE could provide institutions the opportunity to reduce costs while also providing an equally efficacious alternative in stated patient populations.

1 ASP is average selling price (a manufacturer's unit sales of a drug to all purchasers in the United States in a calendar quarter divided by the total number of units of the drug sold by the manufacturer in that same quarter).

2 Centers for Medicare and Medicaid Services, "2017 ASP Drug Pricing Files." cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2017ASPFiles.html, accessed on 23 March 2017.

3 United Kingdom Department of Health, "Clinical Guidelines for Immunoglobulin Use (Second Edition Update)." Updated 15 November 2011, gov.uk/government/publications/clinical-guidelines-for-immunoglobulin-use-second-edition-update, accessed on 28 October 2016.

4 Winters JL, et al., "Cost-Minimization Analysis of the Direct Costs of TPE and IVIg in the Treatment of Guillain-Barré Syndrome." *BMC Health Serv Res* 2011; 11: 101.

5 Chapman S, et al., "Acute Renal Failure and Intravenous Immune Globulin: Occurs With Sucrose-Stabilized, but not With D-Sorbitol-Stabilized, Formulation." *Annals of Pharmacotherapy.* 2004: 38: 2059–2067.

For further reading:

van der Meché FG, Schmitz PI, and the Dutch Gullain-Barré Study Group, "A Randomized Trial Comparing Intravenous Immune Globulin and Plasma Exchange in Guillain-Barré Syndrome." *N Engl J Med* 1992; 326 (17): 1123–1129.

Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group, "Randomised Trial of Plasma Exchange, Intravenous Immunoglobulin, and Combined Treatments in Guillain-Barré Syndrome." *Lancet* 1997; 349 (9047): 225–230.

Sanders DB, et al., "International Consensus Guidance for Management of Myasthenia Gravis. Executive Summary." *Neurology* 2016; 87 (4): 419–425.

Consider working with your hospital to evaluate your treatment processes and costs for using TPE as a treatment for key neuromuscular diseases.

This paper represents one hospital's experience. Published cost comparisons reflect variability in patient populations and methods for calculating costs. Conclusions across studies are inconsistent.

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