**Progress Report:** Date: 8/24/15

**Project:** ASFA Registry Study

To date there has been steady progress since the registry was IRB approved last year. In 2015, there was an amendment to include patients with leukemia as a study group. Currently there are currently 137 patients that have been retrospectively added to the database. These include 17 Neuromyelitis Optica (NMO) patients, 10 Wilson’s disease patients, 15 MUSK positive Myasthenia Gravis patients and 95 leukemia patients. Three abstracts have been submitted, one on the current status of MUSK positive Myasthenia Gravis patient database, (accepted to the AABB 2015 meeting), a second on NMO patient database which was presented as an oral presentation at the April 2015 ASFA national meeting, and a third, presented as a poster, on the use of hetastarch in patients undergoing leukapheresis for leukemia, at the same ASFA meeting. The previous data on Wilson’s disease has been as accepted as a manuscript for JCA. We also anticipate an editorial on the use of the multicenter ASFA registry to gather outcome data in these patients.

**Abstracts**


**Papers**


**Amendments since the last continuing review:**
The study was amended on 3/31/15 (CNMC) to update inclusion and exclusion criteria (including leukemia patients), changes to the assent and consent forms, updating new collaborators involved in study design, data collection and analysis, and updating the name of the ASFA Rare Disease Registry to the ASFA Research Subcommittee throughout the protocol and assent/consent documents.

Respectfully submitted,

Edward Wong, MD
P-04
REPORT OF THE ASFA NEUROMYELITIS OPTICA APERHESIS REGISTRY
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Purpose: Neuromyelitis optica (NMO) is an inflammatory neurologic disease in which approximately 85% of patients have an identified antibody to aquaporin-4. Several anecdotal reports or small cases series have shown encouraging results with therapeutic plasma exchange (TPE), though it has been very difficult to establish its optimal role. The lack of a consistent and comprehensive recording of data can bias or limit apheresis experiences. In order to collect and report apheresis data in a standardized manner, an ASFA REDCap disease registry was developed with the anticipation of providing treatment and prognostic information for this disease.

Methods: The ASFA apheresis registry subcommittee of the Application committee used the REDCap database to collect demographic, clinical information, apheresis procedural information, and treatment schedule outcomes. Therapeutic response was indicated by the degree of improvement in primary relapse symptoms. A review on both prospective and retrospective data was performed on patients with NMO presenting for TPE at five institutions from 2000 to 2013.

Results: This multi-center study includes one pediatric and four adult centers. Based on Census Bureau defined regions, 40% (2/5) and 60% (3/5) of the institutions are located in the Midwest and Northeast, respectively. Seventeen patients have been entered into the NMO registry. Ninety-four percent (16/17) of patients were female and six percent (1/17) were male. The average age of diagnosis was 45 years (range 13 to 66). The average time from diagnosis to first TPE procedure was found to be 1.9 years (range 0 to 12). The most common clinical symptom prior to initiation of TPE was blindness which occurred in 82% (14/17) of patients. All centers reported 1-1.25 plasma volume exchange for each procedure with 100% fluid balance and 5% albumin used as the primary replacement fluid. Fresh frozen plasma was used for two cases after kidney biopsies and normal saline was used as a secondary replacement fluid in 16% (26/162) of the procedures. The average TPE course of treatment (COT) consisted of five exchanges (range three to seven), with patients receiving a mean of 2.5 COT (range one to six). The most common TPE COT was every other day including weekends, with one center reporting one COT of daily TPE, one center reporting one COT of three daily followed by four every other day, and one center reporting two COTs that were maintenance schedules of once per week. A clinical status assessment (from pre-TPE baseline to within ten days of last TPE in a series) showed no improvement in 3% (1/30), mild improvement in 47% (14/30), moderate improvement in 40% (12/30), and marked improvement in 10% (3/30). Forty-three percent (13/30) of COTs reported relapses with an average of ten months (range one to 36) since last TPE.

Conclusions: By establishing a multi-institutional registry for apheresis, we were able to collect a larger amount of data on apheresis experiences with NMO patients. This information enables us to better evaluate the apheresis practice and eventual efficacy for NMO. NMO is a rare disease, however, with increasing clinical awareness and new diagnostic technologies, we will likely see an increase in apheresis requests for these patients in the future. Having a high quality database in which data is collected in a standardized manner and carried out by ASFA, a national organization for Apheresis Medicine, could facilitate a uniform treatment program and provide prognostic information for this disease.

P-05
AN EX VIVO CLINICAL STUDY DEMONSTRATES LIPOPROTEIN APERHESIS REDUCES LEVELS OF CIRCULATING GALECTIN-3
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Introduction: Galectin-3, a beta-galactoside-binding protein, is emerging as an important biomarker, prognostic indicator, and therapeutic target for a wide range of acute and chronic inflammatory conditions and infectious diseases, including cardiovascular disease, autoimmune conditions, diabetes, kidney and liver disease and cancer. Galectin-3 activates inflammatory signaling and stimulates the development and progression of fibrosis as well as metastatic cancer. Research indicates that blocking galectin-3 significantly alters disease progression in target organs and tissues, by reducing inflammatory/fibrotic damage, and pro-metastatic cell signaling. Therefore, galectin-3 is emerging as an important therapeutic target. The galectin-3 ELISA is a FDA approved assessment tool and prognostic indicator for congestive heart failure, with broad clinical utility beyond cardiovascular disease alone.

Purpose: In this presentation, results will be presented of the first pilot clinical study (n = 9/group) evaluating the ability of currently available lipoprotein apheresis (LA) devices to remove excess galectin-3 from human plasma.

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Scale from baseline in the two the treatment groups and were comparable during overall treatment course. The onset of recovery was faster in IVIG group at 2 weeks as compared to 4 weeks in TPE group. Health system cost of treatment in emergency ward was \( \text{Rs} \) 19762(3295) per patient treated and \( \text{Rs} \) 2670(445) per bed day treatment. Total out of pocket cost including Ancillary charges for IVIG group was \( \text{Rs} \) 2,9247(3654 \$) and for TPE group was \( \text{Rs} \) 1,04,070(1734 \$) and found to be statistically significant. As both IVIG and TPE are effective treatments for acute Guillain Barre Syndrome, the use of plasma exchange offers a considerable cost saving in out of pocket cost. ICER of treatment with IVIG as compared to TPE is \( \text{Rs} \) 160528(26755 \$), which implies that incremental cost of treating GBS patients with IVIG as compared to TPE was \( \text{Rs} \) 160528 per unit reduction in GBS disability score.

**Conclusion:** In terms of ICER the treatment of GBS patients with IVIG does not appear to be cost effective in Indian context. However future research on cost effectiveness of GBS treatment using DALY as outcome measure recommended for more robust conclusion.

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**HEPARIN-INDUCED THROMBOCYTOPENIA ASSOCIATED WITH HEMATOPOIETIC PROGENITOR CELL-APHERESIS COLLECTION**

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**Purpose:** Heparin-induced thrombocytopenia type II (HIT) is a potential complication from exposure to unfractionated heparin (UFH) or low-molecular weight heparin (LMWH) and is characterized by thrombocytopenia with an increased risk for thrombosis 4-14 days following exposure. The condition is mediated by the formation of IgG against platelet factor 4 (PF4)/heparin complexes which may lead to platelet activation. We describe two patients who developed HIT and thrombosis after undergoing hematopoietic stem cell-apheresis (HPC-A) collection for autologous transplant.

**Methods:** The medical records of both patients were reviewed retroactively. HPC-A collection was performed with the Cobe Spectra Apheresis System. Per protocol, 6 units UFH per mL. ACD-A was utilized during HPC-A collection in both patients since the pre-procedure platelet count was \( \geq 50,000/\mu L \). HIT polyclonal ELISA was used to detect PF4 antibodies, and heparin induced platelet aggregation was an in-house laboratory developed assay.

**Results:** Patient A is a 63-year-old female with IgA multiple myeloma complicated by a deep venous thrombosis (DVT) treated with UFH 6 months prior to HPC-A collection. She underwent autologous HPC-A collection for 2 days with a total UFH dose of 9,780 units in preparation for transplantation. Three days following HPC-A collection, she developed severe thrombocytopenia (8,000/µL) and a right internal jugular vein thrombus. PF4 antibodies were significantly elevated by ELISA (OD 1.8, reference <0.4), heparin induced platelet aggregation testing was consistent with the presence of PF4 antibody, and HIT was diagnosed. Following argatroban and fondaparinux therapy in conjunction with complete platelet count recovery (200,000/µL), autologous transplant was performed after 4 treatments of therapeutic plasma exchange (TPE) with 1.0 plasma volume replaced with 5% albumin to remove PF4 antibodies over an 8-day period, washing of the HPC-A product to remove any heparin, and treatment with intravenous immunoglobulin and argatroban on the day of transplant. An 80% reduction of PF4 antibodies was achieved prior to infusion of the HPC-A product. Other than delayed engraftment and engraftment syndrome, her post-transplant course was unremarkable and there was no evidence of thrombosis.

Patient B is a 67-year-old male with lambda light-chain AL amyloidosis who developed a DVT and was treated with LMWH several months prior to HPC-A collection. HPC collection was performed for 2 days with a total UFH dose of 18,378 units. He developed thrombocytopenia 2 days after HPC-A collection (41,000/µL) and a DVT 7 days post-collection, was treated with UFH, and presented with a pulmonary embolus and numerous venous thromboses 4 days later. He was diagnosed with HIT based on elevated PF4 antibodies (OD 2.057) and a positive serotonin release assay. PF4 antibodies were undetectable at the time of HPC-A transplant 5 months later, he did not require peri-transplant TPE, and his post-transplant course was uneventful.

**Conclusion:** Both patients discussed presented with HIT shortly after receiving UFH during HPC-A collections after having had exposures to UFH in the past, suggesting that the UFH used in these collections contributed to this complication. Given that UFH is routinely used during HPC-A collection, these cases emphasize the importance of considering HIT in patients with thrombocytopenia and thrombosis following UFH use with HPC-A collection.

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**USE OF HYDROXYETHYL STARCH IN LEUKOCYTHERAPESIS PROCEDURES DOES NOT INCREASE RENAL TOXICITY**

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USE OF A MODIFIED BLOOD PRIME WITH THE THERAKOS™ CELLEX® PHOTOPHERESIS SYSTEM TO MINIMIZE BLOOD DONOR EXPOSURES AND RED CELL GAIN IN 2 PEDIATRIC PATIENTS

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Purpose: The Therakos™ Cellex® Photopheresis System is a single, integrated closed system device used for the delivery of extracorporeal photopheresis (ECP). For pediatric patients treated with the Cellex® system, a blood prime is recommended when the estimated extracorporeal blood volume of the device exceeds 10–15% of a patient’s total blood volume. The blood prime procedure provided by the manufacturer requires a packed red cell unit of at least 300 ml in volume to perform for each procedure. At the end of the blood prime procedure, 20 ml of the return bag is returned to the patient that can result in a variable net gain or loss in red blood cells depending on the starting hematocrit of the packed red cell unit. At Phoenix Childrens Hospital, two pediatric patients presented for ECP treatment for complications of GVHD. One with a history of chronic iron overload, the other with an increased allergic sensitivity to blood products. In an attempt to minimize exposure to multiple blood products and have better control over potential red cell gain from a standard blood prime, both patients received a modified blood prime with their procedures. This modified blood prime utilizes one packed red cell unit split evenly for two procedures and its use allows for more control over red cell loss and gain.

Methods: The modification in blood prime was performed on a 13 year old male and 7 year old female with weights of 29 kg and 20 kg, respectively. The modified blood prime procedure utilized half of a packed RBC unit with volume between 150–225 ml. Split units less than 225 ml were brought up to a volume of 225 ml with normal saline and then a HCT was performed to allow for the calculation of RBC volume introduced.
CONTROL ID: 2273367

TITLE: Report of the ASFA Apheresis Registry on Muscle Specific Kinase Antibody Positive Myasthenia Gravis

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PRESENTATION TYPE: Oral or Poster Presentation

CURRENT CATEGORY: Scientific

ABSTRACT BODY:

Background/Ca se Studies: Anti-muscle specific kinase antibody (MuSK Ab) positive myasthenia gravis patients (MG Pts) are known to have different clinical course compared to acetylcholine receptor (AchR) Ab MG Pts. Therapeutic plasma exchange (TPE) is reported to be effective for these Pts, however, little is known of the response and of how TPE is performed. The ASFA apheresis registry was developed to analyze both outcome and procedural data in response to TPE.

Study Design/Methods: The multi-institutional ASFA apheresis registry study using a REDCap electronic database was used to store detailed un-identified patients' demographic and clinical information, apheresis procedural information, treatment schedules, and treatment outcome/complications. The symptomatic improvement was evaluated by apheresis physicians or neurologists in each facility. All participating sites had obtained local IRB approval, and collected data was analyzed in aggregate.

Results/Findings: As of 3/31/15, a total of 15 MuSK Ab positive MG Pts, 13 female/2 male, median age 44, in 3 centers treated for exacerbation of MG symptoms between 2006 to 2013 have been entered into the registry. Two of the 15 Pts also had AchR Ab and one of them underwent thymectomy. In summary, 30 TPE courses (median 5 TPE/course), a total of 145 procedures, were evaluated. The vast majority of TPE procedures were performed with albumin (Ab) replacement and citrate anticoagulation with 1-1.25 plasma volume exchange in 100% fluid balance. Calcium was added to Ab in 2 facilities and given orally as needed in 1 facility. TPE was performed every other day in 55% of courses, twice per week in 28%, daily in 10% and weekly in 7%. Peripheral vein was used in 50% of courses, central line in 46% and fistula in 4%. 10 Pts (67%) experienced one or multiple relapses after the last TPE with median duration of 7 weeks. The occurrence of pre-TPE objective symptoms and improvement rate after TPE courses is shown in Table. Moderate to full subjective improvement was achieved by 1 TPE in 24%, 2 TPE in 38%, 3 TPE in 59%, 4 TPE in 73% and >4 TPE in 55% with poor responders, overall 94% improvement with mild improvement. Prednisone was decreased after a TPE course in 22% and pyridostigmine in 36%. Adverse events occurred in 3.4% of procedures.

Conclusion: This is the first multicenter registry study to evaluate demographic/clinical/TPE procedure data in MuSK Ab positive MG Pts. The overall subjective improvement was 94% after one course of TPE. 4 TPE may be adequate in one course with additional TPE option. Additional data from multiple other facilities may provide more accurate information.