The use of Heparin Prime followed by Acid-Citrate-Dextrose-Adenine (ACD-A) for Extracorporeal Photopheresis (ECP) using the CELLEX ® instrument.

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BACKGROUND: ECP is an immune-modulatory procedure currently used for treating Graft vs. Host Disease (GVHD), Cutaneous T-Cell Lymphoma (CTCL), SézarySyndrome as well as solid organ rejection. Briefly, access is obtained through a large vein, or central line or port capable of sustaining a flow of 50ml/min. Whole blood is drawn by the instrument and mixed with anticoagulant. 1500ml of blood is processed and the buffy coat is collected and treated with 8-methoxypsoralem (8-MOP) and exposed to 2 Joules / cm^2 of UVA light in a transparent flat plate and then returned to the patient. 8MOP binds irreversibly to DNA once exposed to UV light and the cells are returned to the patient. These cells will undergo apoptosis and crypto-antigens will be processed & presented to T-Cells. which then mount an immune response to tumor antigens. The manufacturer recommends the use of high dose of unfractionated heparin (10.000 Units) for the procedure. Large doses of heparin can lead to significant bleeding in patients who are thrombocytopenic and has been shown to cause Heparin Induced Thrombocytopenia. Heparin has a half-life of 4 hours. ACDA is short lived and is removed from circulation by the liver where citrate is rapidly converted to bicarbonate as part of the Krebs' cycle.

HYPOTHESIS: ACDA has a long safety track record and is the anticoagulant of choice for therapeutic apheresis procedures, (plasmapheresis, leukoreduction, thrombocytoreduction), as well as peripheral blood stem cell collection. Using citrate anticoagulation for ECP should be efficient in preventing coagulation during ECP and minimize exposure to heparin.

METHODS:

A total of 82 procedures were reviewed.
A CBC and extended chemistry panel including ionized calcium and magnesium were drawn before the procedure. The Cellex® ECP instrument was setup using the manufacturer's disposable sterile kit. The circuit was primed with heparin in saline. The patient's port access site was treated with EMLA® cream 30 minutes prior to access in order to achieve topical anesthesia. The port site packed with high dose heparin (1000 units/ml) was accessed with and the packing anticoagulant was removed. The access line from the ECP apparatus was then connected to the port. The bag of heparin/saline used for priming was then removed and replaced with ACDA. The procedure was started and conducted solely with ACDA for anticoagulation. Flow rate was maintained under 50ml / minute during the entire procedure. Once 1500ml of whole blood were processed, the operator was prompted to add a calculated volume of 8-MOP to buffy coat collection bag. The buffy coat was then irradiated with UVA to achieve a dose of 2 Joules/cm^2 . Once this dose was achieved, the buffy coat was returned to the patient. The patient was then disconnected from the equipment and the port was packed according to manufacturer's specification. The patient was discharged and reminded of UV precautions namely avoid exposure of skin & eyes to sunlight for the following 24 hours.

RESULTS:
A total of 45 procedures in patients with a diagnosis of CTCL and 37 procedures were reviewed in patients with GVHD. The results are shown in the table below. Heparin was mixed in saline and the patient received the heparin/saline prime. The anticoagulant was changed from heparin/saline to ACDA for the rest of the procedure. There were two kit failures in the series, both in patients with GVHD or CTCL.. All patients received significantly less heparin than indicated by the manufacturer (10.000 Units) and successfully completed the procedure without clotting the circuit. Electrolytes were corrected during the procedure and initial ionized calcium was used to gauge theneed for supplemental calcium.

When required, additional calcium was given PO. IV calcium calcium gluconate was available & given in a separate access site when necessary,so as not to form clot in the ECP circuit. Overall citrate toxicity was not frequent in the series analyzed; when it occurred, it was mild and resolved by pausing the procedure and oral calcium.

	Buffy Coat processed	Anticoagulant to patient	ACDA to patient	Units of heparin to patient	Buffy coat treated	UVA irradiation min.	Duration hours	Fluid Balance
CTCL	1560ml	232ml	141ml	1555	97.89	18:40	2:05	+332
GVHD	1463 ml	235 ml	139ml	1389	91	20:00	2:20	+320

Conclusion:

Using heparin prime followed by citrate anticoagulation has become the standard practice at our institution. We have shown this to be a safe and efficient method for anticoagulation, avoiding risks of bleeding associated with high doses of heparin.