

12-2015

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Recommended Citation

Sisk, Bryan A., "Guidelines for use of extracorporeal photopheresis in acute graft-versus-host disease (GVHD)" (2015). *Kidneycentric*. Paper 11.
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Guidelines for Use of Extracorporeal Photopheresis in Acute Graft-Versus-Host Disease (GVHD)

Bryan Sisk, MD

7/18/2015

History: The first investigational study on the use of extracorporeal photopheresis (ECP) was published in 1987, and focused on treatment of cutaneous T-cell lymphoma.¹ This study led the FDA to approve of photopheresis. Although T-cell lymphoma is the only FDA approved indication for photopheresis its therapeutic use has expanded to a number of other disease processes, most notably acute and chronic graft versus host disease (GVHD).

Photopheresis Procedure: ECP is a leukapheresis-based therapy. Whole blood is processed outside of the body in the following way: whole blood is drawn from a catheter placed in a central vein; using centrifugation the different constituents of blood are separated based upon density i.e. white blood cells (WBC) separate into the buffy coat which can distinguished from red blood cells (RBCs) and plasma.² The RBCs and plasma are returned to the patient, but the buffy coat containing the WBCs is isolated (it should be noted that only 5-10% of the patients WBCs are typically captured during the procedure). Thereafter, 8-methoxypsoralen (8-MOP) is added directly to buffy coat; WBCs mixed with the psoralen 8-MOP, are exposed to UVA light; the buffycoat with the WBCs are returned to the patient and the procedure is completed.

Mechanism of Action of Photopheresis: “Although ECP has been in clinical use for more than 25 years and is widely used for a variety of clinical entities, the mode of action remains elusive.”² There has been minimal investigation into the mechanism since the 1980s. While it is known that 8-MOP leads to DNA crosslinking and WBC apoptosis, this mechanism alone is insufficient to explain the clinical/therapeutic effects of ECP. More recently, it has been found that ECP leads to an increase in CD4+ CD25+ T-regulatory T-cells, which are important for regulating and preventing autoimmunity. Therefore an alternative hypothesis from induced cellular apoptosis is that ECP releases a milieu of cytokines that decrease autoimmunity without increasing risk of opportunistic infections.

Conditions Treated: ECP has been utilized in treatment of cutaneous T-cell lymphoma, acute and chronic GVHD, scleroderma, solid organ transplant, Crohn’s disease, atopic dermatitis, type-1 diabetes mellitus, pemphigus, epidermolysis bullosa acquisita, erosive lichen planus, and systemic lupus erythematosus.

Recommendations for Acute GVHD: ECP is currently recommended as second line therapy for patients with acute GVHD, grade II – IV disease who are steroid refractory, steroid dependent or steroid intolerant.³ Infective causes of diarrhea should be excluded, though acute GVHD can be concomitant with infection. Two treatments/procedures of photopheresis on separate days should be initiated

weekly for a minimum of eight cycles (8 weeks). Patients with grade IV aGVHD may benefit from three treatments per week for the first 4 weeks. Patients who have progressive aGVHD during this time may require additional therapy at the discretion of the treating physician. Our center recommends this initial course of therapy for progressive/refractory chronic GVHD too.

References

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