CHAPTER 40

EXTRACORPOREAL PHOTOCHEMOTERAPY (ECP) IN DERMATOLOGY

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INTRODUCTION

Extracorporeal photochemotherapy (ECP, photopheresis) is a treatment method which includes ex vivo exposure of mononuclear cells to photo activated 8-methoxypsoralen (8MOP) and reinfusion to the patient.[1] Although 5-10% of mononuclear cells is influenced in the procedure the treatment has long-lasting immune-modulatory effects by induction of tolerance of regulatory T cells. ECP is reported to be effective for wide variety of diseases such as cutaneous T cell lymphoma, autoimmune diseases, graft versus host disease and organ graft rejection.

ECP is advantageous since the low frequency of side effects related to treatment however high treatment costs and practical efforts that required make ECP to be less perceived.[2] The treatment of ECP is usually well-tolerated and no severe World Health Organization grade III-IV side effects have been reported. Side effects during procedure may be transient hypotension, mild anemia and/or thrombocytopenia. The patients who are not suitable for treatment of ECP: known sensitivity to psoralen, pregnant, history of heparin-induced thrombocytopenia, unsatisfactory cardio-circulatory function and low hematocrit values.[3]

HISTORY

US Food and Drug Administration (FDA) had approved ECP for treatment of cutaneous T cell lymphoma (CTCL) in 1988 after Edelson et al. published a manuscript in New England Journal of Medicine entitled 'Treatment of Cutaneous T-Cell Lymphoma by Extracorporeal Photochemotherapy'.[4] In 1998, Becherel et al successfully treated erosive oral lichen planus and showed effectiveness of ECP in autoimmune diseases concurrently prevention of cardiac transplant rejection by Barr and Dall'Amico.[5,6]

Original ECP technique was modified by French group so called French method of ECP which includes collection of highly enriched mononuclear cells (MNC) by continuous flow separator (Spectra, COBE lab), transferring cells into UV-A permeable bag (Macopharma) and addition of 8MOP to the bag and irradiation of UV-a with UV-Matic irradiator (Vilbert-Lourmat).[1] Later Sniescinski et al. collected MNC with continuous flow separator and irradiated cells with Johnson and Johnson device. The first use of ECP in acute and chronic graft versus host disease (GVHD) was demonstrated by her group.[7]

TECHNICAL ASPECTS

Currently, there are two approaches are used in ECP treatments: inline and off-line ECP system. 'In-line' system is a fully integrated and closed method ('one step method') where the separation of mononuclear cells, 8-MOP photo-activation with UV-A and reinfusion of the cells take place in. The most important advantages of this technology includes the minimum risk of bacterial contamination. Disadvantages of the system are large extracorporeal volume is dependent on weight and volume percentage of red blood cells and non-uniform cell irradiation.[1] 'Off-line' system (open or 'two-step method') contains a continuous flow cell separator and a separate device for cell irradiation. This system enables to perform ECP in patients with very low body weight and control the quality at every step of the procedure. However this system has not been approved by FDA for use in ECP and patient reinfusion errors can not be detected (Table 1).[1]

MECHANISM OF ACTION

Many studies were conducted to discover the mechanism of action of ECP however it has been still not well defined. ECP is composed of three steps: Collection of the buffy coat fraction, incubation of cells with 8-MOP, followed by irritation with UVA and reinfusion of cells into the patients.[2] 8-MOP and UV-A affects the cellular components. UV-A with wavelength ranging between 329 to 400nm activates 8-MOP which is responsible of DNA cross-linking with pyrimidine bases, binding to cytosolic proteins, cell membrane damage with some antigenic modifications and finally the apoptotic cell death.[8]

After reinfusion the apoptotic leukocytes that are retained in spleen, liver, small intestine and lymph nodes initiate to express apoptotic cell molecular patterns and are removed from the body by resident antigen presenting cells (APCs). Clearance of apoptotic

SUMMARY

Technical improvements and recent findings in disease pathophysiology ECP has become an accepted approach in GVHD and CTCL in hematology. ECP induces tolerance via Tregs. ECP is safe and applicable in all patients even with low body weight and poor clinical conditions. The optimal schedule and the length of treatment are still unknown. After the mechanisms of action of ECP have been fully distinguished as well as additional clinical studies and long-term follow-up results have been evaluated, the role of ECP will expand in the future.

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