

LETTER TO THE EDITOR

Long term follow-up results on severe recalcitrant atopic dermatitis treated with extracorporeal photochemotherapy

Editor

Extracorporeal photochemotherapy (ECP) has shown to be effective in a series of relatively small studies (Table 1) conducted on patients with severe chronic atopic dermatitis (SAD) recalcitrant to traditional first and second line therapies.^{1–8} The purpose of our study was to see if ECP could have a role in the long term treatment of the disease (at least 2 years) in patients with SAD recalcitrant to traditional therapies for more than 6 months.

All clinical investigation was conducted according to Declaration of Helsinki principles. Approval was granted by the ethics committee and informed consent was obtained from all patients for the experimental procedures. The study, a retrospective follow-up based on a review of clinical files, was conducted at the Department of Clinical Medicine and Immunological Science, University of Siena, between January 2006 and December 2011. All the patients had a long history (mean 40.2 years) of SAD (Table 2). ECP was performed using three different UVAR devices (Therakos Inc., West Chester, PA, USA) according to previously described methods.⁹ Patients returned every 2 weeks in the first 3 months (12 weeks) after which the frequency of treatment was modified according to clinical response. In particular, intervals were prolonged during maintenance therapy after clinical improvement. All of the patients received at least 24 cycles of ECP. Data registered in our review of the patient files are reported in Table 2. Clinical records were made at each visit, at 3, 6, 12 months and every 6th month after that. The SCORAD standardized system was employed to quantify the extent of skin lesions and severity of SAD. Pretreatment SCORAD was between 78 and 85 reflecting severe generalized or erythrodermic AD (Table 2). The efficacy of ECP was considered essential when the SCORAD index decreased significantly after the start of ECP and when the dose of immunosuppressants could be reduced by at least 50% with respect to initial therapy. Clearance was defined as SCORAD improvement of at least 75% from the baseline. ECP was considered inefficient when patients remained in a persistent active stage, when it was necessary to increase the dose of immunosuppressants or when immunosuppressants could not be reduced by more than 50%.

Table 1 Studies in the literature where ECP was used in patients with atopic dermatitis

Authors	Patients	ECP cycles	Responders/ all patients	Assessment of treatment response
Prinz <i>et al.</i> ¹	3	6–12	3/3	Clinical evaluation, total IgE
Richter <i>et al.</i> ²	3	10	2/3	Costa's score, total IgE, ECP
Prinz <i>et al.</i> ³	14	>6	10/14	Clinical evaluation, total IgE, ECP, CD4/CD8
Radenhausen <i>et al.</i> ⁵	10	10	10/10	SCORAD ECP, sE-selectin, sIL-2R
Radenhausen <i>et al.</i> ⁶	30	6–10	24/30	SCORAD total IgE, ECP, sE-selectin, sIL-2R.
Sand <i>et al.</i> ⁷	7	>6	7/7	SCORAD, SF-36 quality of life index
Mohla <i>et al.</i> ⁴	1	6	1/1	Disease specific quality of life index
Hjuler <i>et al.</i> ⁸	6	6–80	6/6	Clinical course
Rubegni <i>et al.</i>	7	12–100	6/7	SCORAD, total IgE, concomitant immunosuppressive therapy

ECP, extracorporeal photochemotherapy.

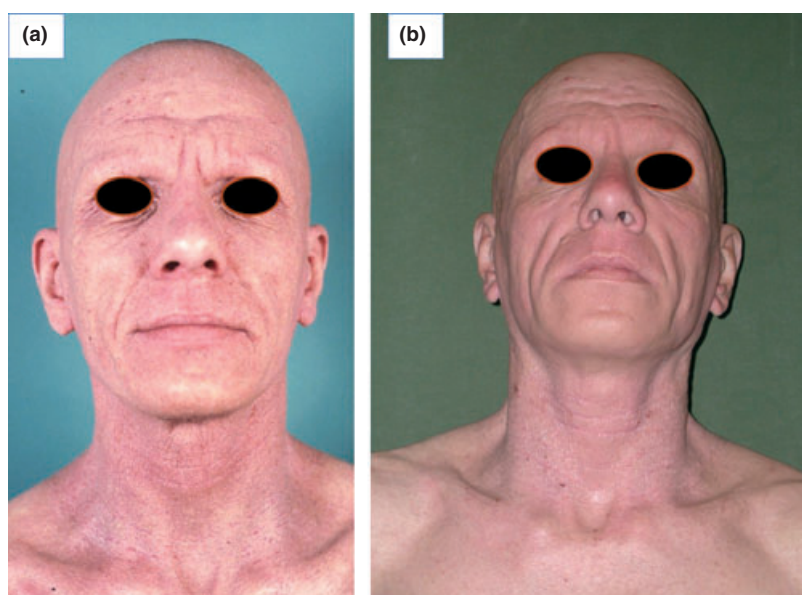
Multivariate analysis of variance (MANOVA) for repeated measures was used to evaluate the statistical significance of time-changes in the SCORAD index and total IgE.¹⁰ Population means from MANOVA were also estimated together with their 95% confidence intervals. A statistical significance level of 95% ($P < 0.05$) was considered. MANOVA statistical computations were performed using SPSS software.

The results are summarized in Table 2. No adverse events were encountered during the study and ECP was well tolerated by all patients (Fig. 1). The contribution of ECP at two year follow up was essential in 6/7 patients (85.7%). As previously reported, a distinct reduction of SCORAD, and in particular pruritus, was evident after 3–6 cycles (2–3 months).⁸ Figure 2 shows that SCORAD confirmed a statistically significant decrease from the beginning of ECP to 24 months later (MANOVA test, $P < 0.05$). In particular, 95% confidence levels of estimated means indicate that the highest decrease of SCORAD index with respect to initial time occurred just after three months. SCORAD mean reduced significantly to about one third after one year and to about one fifth after 2 years when a null value was observed in two out of seven

Table 2 Clinical and anamnestic data of our study population. Response to ECP, treatment frequency, concomitant therapies and IgE serum levels

Patients/Age/Sex Duration disease Concomitant disorders	Concomitant treatments SCORAD IgE (U/mL) ECP frequency Start of ECP	Concomitant treatments SCORAD IgE (U/mL) ECP frequency 3 months	Concomitant treatments SCORAD IgE (U/mL) ECP frequency 6 months	Concomitant treatments SCORAD IgE (U/mL) ECP frequency 12 months	Concomitant treatments SCORAD IgE (U/mL) ECP frequency 24 months
1/19/M 18 None	CyA: 3.5 mg/kg 84 1865 U/mL 2 weeks	CyA:3.5 mg/kg 56 1436 2 weeks	CyA:3 mg/kg 40 1560 4 weeks	CyA:1 mg/kg 31 1200 8 weeks	CyA:None 21 800 8 weeks
2/38/F 35 Diabetes	CyA: 3.5 mg/kg 78 896 2 weeks	CyA: 3 mg/kg 44 1483 2 weeks	CyA: 2,5 mg/kg 39 425 4 weeks	None 20 890 6 weeks	None 21 800 12 weeks
3/75/M 72 Chronic renal failure	None 85 1100 2 weeks	None 765 900 2 weeks	None 54 1345 4 weeks	None 32 1200 8 weeks	None 25 890 8 weeks
4/29/F 25 Crohn's disease	CyA: 3.5 mg/kg 83 2225 2 weeks	CyA: 3.5 mg/kg 78 2200 2 weeks	CyA: 3.5 mg/kg 78 2230 2 weeks	Dropped out	Dropped out
5/50/M 50 Alopecia universalis	6 metilprednis: 16 mg 79 >5000 2 weeks	6 metilprednis: 16 mg 58 >5000 2 weeks	6 metilprednis: 12 mg 41 >5000 4 weeks	6 metilprednis: 8 mg 28 >5000 2 weeks	6 metilprednis: 4 mg 26 > 5000 8–12 weeks
6/37/F 37 Solar urticaria, milk allergy	6 metilprednis: 16 mg 81 >5000 2 weeks	6 metilprednis: 16 mg 50 >5000 2 weeks	6 metilprednis: 12 mg 41 >5000 4 weeks	6 metilprednis: 8 mg 28 >5000 2 weeks	6 metilprednis: 4 mg 26 > 5000 8–12 weeks
7/50/F 45 None	None 80 832 2 weeks	None 49 600 4 weeks	None 36 280 4 weeks	None 25 203 6–8 weeks	None 0 98 8–12 weeks

ECP, extracorporeal photochemotherapy.

**Figure 1** (a) Patient 5 at the beginning of extracorporeal photochemotherapy treatment (SCORAD = 79; IgE >5000). (b) Patient 5 after the first year of treatment (SCORAD = 28; IgE >5000).

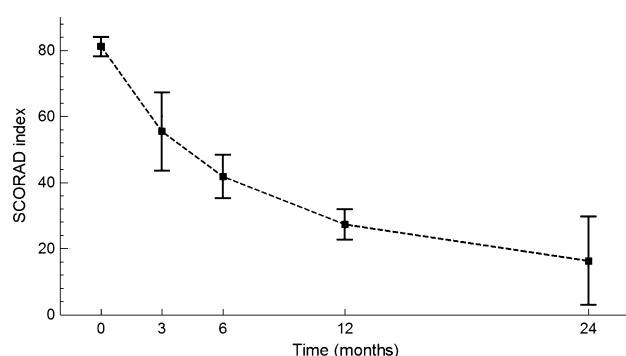


Figure 2 Time behaviour of estimated mean SCORAD index and the related 95% confidence intervals. MANOVA test: estimated means and 95% confidence intervals (CI) of SCORAD index and IgE value.

patients. We observed fluctuant levels of serum IgE in almost all patients (Table 2) which did not correlate with the clinical response (MANOVA test, $P > 0.05$). Previous studies (Table 1) indicated that almost 65% of patients achieved partial or complete remission of SAD within 10 cycles of ECP used at 2 or 4 week intervals.^{7,8}

In our study, we obtained a long lasting stabilization effect (of about 2 months) in almost all the responders instead of 20%.⁶ However, this stabilization was obtained after the first year of treatment in 4/7 patients (57.1%). On these bases, we can speculate that the long term stabilization effect due to ECP in some patients can be obtained after a greater number of cycles. In fact, treatments every 2–3 months achieved good maintenance without the need of other immunosuppressive drugs. A relapse of the disease only occurred in patient 6 who temporarily suspended ECP and may be related to the anaphylactic shock that she experienced.

In conclusion, our study confirms that ECP, in particular when used as a long term treatment, can be a safe, effective treatment in patients with SAD resistant to previous therapies.

P. Rubegni,[†] S. Poggiali,^{†,*} G. Cevenini,[§] G. D'Ascenzo,[†] A. Perrone,[‡] M.L. Flori,[†] P. Barbini,[§] M. Fimiani[†]

[†]Department of Clinical Medicine and Immunological Sciences, Section of Dermatology, [‡]Department of Clinical Medicine and Immunological Sciences, Section of Pneumology, [§]Department of Cardiac Surgery and Biomedical Technology, University of Siena, Italy

*Correspondence: S. Poggiali. E-mail: sarapog@inwind.it

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