INVESTIGATION

C-reactive protein serum level in patients with psoriasis before and after treatment with narrow-band ultraviolet B*

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Abstract: Background: C-reactive protein is an inflammatory biomarker and its level increases in the serum of psoriatic patients. Its level is also associated with Psoriasis Area and Severity Index score.
Objective: The aim of this study was to assess the decrement of serum C-reactive protein level with narrow-band ultraviolet B (NB-UVB) therapy.
Methods: C-reactive protein serum levels in psoriasis patients were measured before and after treatment with NB-UVB and the data were analyzed in relation to the Psoriasis Area and Severity Index score improvement.
Results: Baseline C-reactive protein levels among psoriatic patients were higher than normal. These levels decreased significantly after treatment (P<0.001). At the beginning of the study, patients with higher levels of C-reactive protein also had more extensive and severe skin involvement. The highest decrease in C-reactive protein was observed in patients who responded better to the treatment and achieved a higher Psoriasis Area and Severity Index 75%. There was an association between baseline Psoriasis Area and Severity Index scores and C-reactive protein levels.
Conclusion: Patients with moderate to severe plaque-type psoriasis had active systemic inflammation, which was demonstrated by increased levels of C-reactive protein. Furthermore, skin disease severity was correlated with C-reactive protein levels. Phototherapy healed the psoriatic skin lesions and reduced inflammation, while decreasing C-reactive protein levels.
Keywords: C-Reactive Protein; Psoriasis; Ultraviolet therapy

INTRODUCTION

Chronic plaque psoriasis is the most common type of psoriasis. It is estimated that the prevalence of psoriasis is 2%-5% worldwide. However, in Asia alone, the prevalence is 0.4%-0.7%. Psoriasis is determined by excessive proliferation and impaired evolution of keratinocytes. Due to its recurrent nature, psoriasis has a major impact on the patient's quality of life.[1] Phototherapy represents a mainstay treatment for psoriasis vulgaris. Psoriasis lesions can be healed by the narrow band ultraviolet B lights (NB-UVB) at a length of 311 nanometers, which has more impact than broadband ultraviolet over a short period; with only a 10% incidence of burning, compared with 28% for conventionally treated patients.[2]

Psoriasis also has an inflammatory nature that is demonstrated by excessive secretion of dermal, systemic, pre-inflammatory cytokines such as IL-2, IL-6,IL-12, IL8, IL-17, IL-19, IL-20, IL-22, IL-23, IL-24, IFN-γ and TNF-α.[3] Furthermore, liver stimulation and the production of acute phase reactants such as C-reactive protein (CRP), which is considered an inflammatory biomarker, are believed to stem from IL-6 secretion induced by TNF-α.[4] CRP is an acute phase reaction protein biomarker that is identifiable within 24 to 48 hours after tissue damage or infection. CRP indicates 6 to 8 hours of half-life and has a wide dynamic range used as an important marker in clinical studies,reducing with a successful treatment. Moreover, assessing CRP serum values is a suitable, daily monitoring method, which can display a clear perspective of events occurring over the preceding 12 hours. The systemic inflammatory pathways may guide treatment of the disease. Thus, new studies must focus on the new mediators that can be found as new therapeutic targets.[5,6] For all the aforementioned reasons, we chose to assess the patients' CRP serum levels to evaluate therapeutic response.

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METHODS

This clinical trial was conducted in individuals suffering from plaque psoriasis who were referred to the Farshchian Hospital, Hamadan, Iran, between March 2009 and March 2010. All of them were included in the study. Participating in this study was voluntary for the patients because it was inconsequential to their treatment. Patients who did not wish to complete the project were allowed to leave the study and subsequently excluded. Because participation was voluntary, refusal to participate involved no penalty or loss of benefits to which the subjects were otherwise entitled, and the subjects were permitted to discontinue participation at any time without penalty or loss of benefits to which the subjects were otherwise entitled. In sum, 30 patients started the study but 5 patients were excluded. Thus, the study continued with 25 cases of plaque type psoriasis. This study was confirmed with the ethical guidelines of the 1975 Declaration of Helsinki. An institutional review board approved the research. The variables investigated in this study were: patients' CRP serum levels, pre- and post-phototherapy serum levels, pre- and post- treatment PSAI scores, the mean of CRP serum value changes pre- and post-treatment, and the PASI 75% value.

All participants were interviewed by a dermatologist and underwent physical examinations. A questionnaire was completed, providing information such as: age, sex, percentage of body surface area involved, intensity level, arrhythmia, skin thickness and skin shedding (desquamation) within the areas affected, pre- and post-treatment CRP serum levels, pre- and post-treatment PASI scores, the number of required treatment sessions and the cumulative doses of radiation emitted to patients to remove 75% of lesions.

CRP serum levels were assessed pre-treatment, following 25 treatment sessions and whenever patients indicated an improvement in skin lesions. After centrifuging blood samples and separating the serum, they were stored at -18°C and all dual samples (taken before and after treatment) were analyzed. Pre- and post-treatment CRP serum levels and their variation were calculated and recorded in the questionnaire. To evaluate CRP serum levels, Minineph Human C-Reactive Protein Kit (Product Code: ZK044. L.R) was used, which took CRP serum values of under 3.8mg as normal.

In this study, we assessed psoriasis severity based on PASI scores and the pre- and post-treatment scores. Finally, the difference between the initial PASI score and the final score was determined and PASI 75% was calculated based on Formula 1.

(Formula 1: how to calculate the lesion recovery rates: PASI % = ($PASI_1$ - $PASI_2$) / $PASI_1$ * 100).

Phototherapy was conducted three times a week, using a wavelength of 311nm to treat the psoriatic lesions of patients with the first dose of 4% J/cm^2. According to the predicted protocol from the skin department, the dose increased gradually, as shown in table 1.

Statistical analyses were performed based on initial and final CRP serum values, their changes pre- and post-treatment, and clinical criteria for determining PASI scores pre- and post- treatment. At the end, the pair T test and Spearman correlation coefficient were used to compare the means, to express the relations between variables and frequency via the data description approach.

RESULTS

In total, out of 25 patients, there were 18 males (72%) and seven females (28%). They were treated by NB-UVB therapy. The ages of these patients ranged from 21 to 67 years, with a mean age of 41.08±14.60 years. All the results obtained are summarized in table 2. Our findings suggested that 16 patients achieved a 75% or more reduction in their PASI score from baseline. The maximum, minimum and mean pre-treatment CRP serum levels were 18.580 mg/l, 2.10 mg/l and 5.79±3.62 mg/l, respectively. Meanwhile, the maximum, minimum and mean pre-treatment PASI scores were 53.10, 9.10 and 22.20±11.51, respectively. However, the maximum, minimum and mean post-treatment CRP levels were 6.88mg/l,

Table 2: CRP serum levels and the PASI scores in 25 patients pre- and post-treatment with NB-UBV

CRP 1	5.79744
CRP 2	3.30132
ΔCRP	2.53612
PASI 1	22.2000
PASI 2	5.2720
PASI 75%	74.9040
Mean number of treatments	22.24
Mean cumulative doses of NB-UVB	42.5804

Table 1: Treatment protocol for phototherapy using NB-UVB in psoriasis patients

Initial Dose		→	0.4 J/cm^2
Frequency of treatment		→	Thrice weekly
	Skin response		**Adjustment**
Subsequent doses	No erythema	→	Increase by 30%
	Minimal erythema	→	Increase by 20%
	Persistent asymptomatic erythema	→	No increase
	Painful erythema with or without edema or blistering	→	No treatment until symptoms subside
	After resolution of symptoms	→	Reduction of last dose by 50%, further increase by 10%
The end of treatment	After the 25th treatment session or whenever the PASI score improves by 75%.		

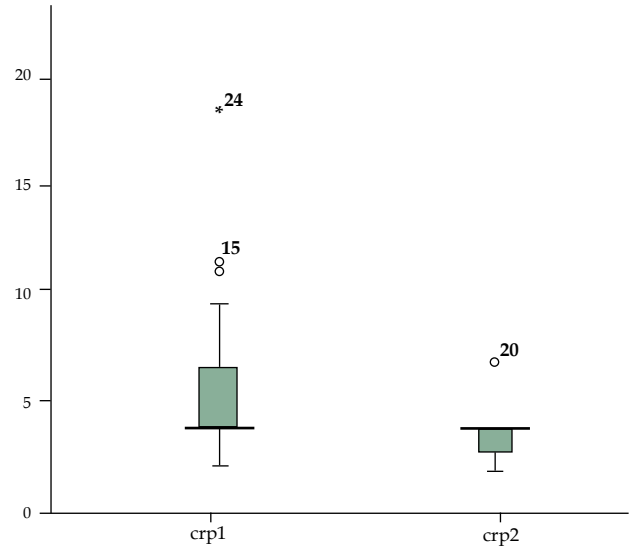
1/80mg/l, and 3.30±1.06, respectively. Furthermore, the maximum, minimum and mean post-treatment PASI scores were 15.00, 00.00 and 5.27±3.92, respectively.

The variation values observed for pre- and post-treatment CRP serum levels are displayed in graph 1.

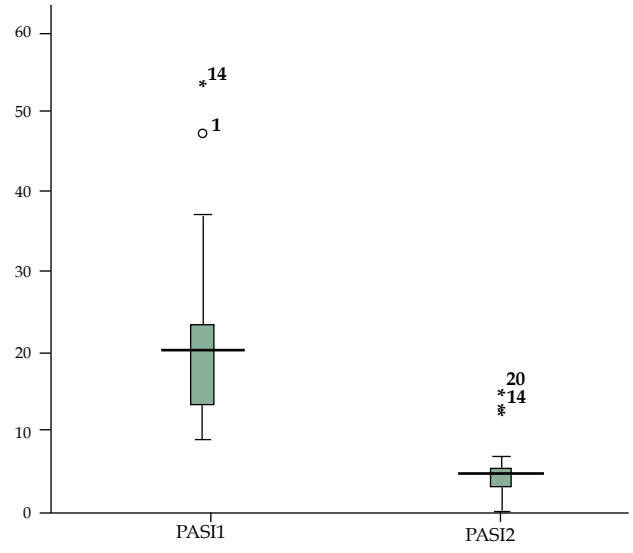
Pre- and post-treatment PASI scores, along with the relationship between post-treatment CRP serum levels and PASI 75%, are shown in graph 2 and graph 3, respectively.

DISCUSSION

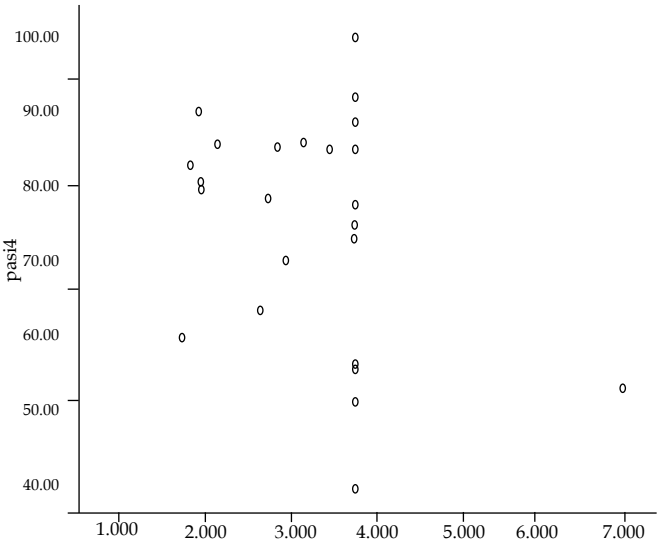
CRP is an acute phase reactive protein, known as a systemic inflammatory biomarker. Serwin reported increased CRP concentrations in active psoriasis.[7] Uysal *et al.* identified CRP as a marker for psoriasis severity.[5] Isha found that CRP levels increased by more than 20 times in psoriasis patients compared with the healthy individuals. After 12 weeks of treatment, it fell to nearly 50% of the initial value.[8] Similarly, we observed a significant decrease in post-treatment CRP serum levels due to NB-UVB phototherapy (P<0.001).



Graph 1: Comparison of CRP serum levels in 25 patients before and after treatment by NB-UVB



Graph 2: Comparison of PASI scores in 25 patients before and after treatment using NB-UVB



Graph 3: The relationship between CRP serum levels in 25 patients, pre- and post-treatment using NBUVB and PASI 75%

In a study conducted in 70 psoriasis patients, Biljan *et al.* observed that inflammatory parameters such as CRP serum levels were significantly related to the clinical demonstrations of psoriasis (p<0.005). They also identified a relationship between disease severity and the increased levels of inflammatory reactions.[9]

In a cross-sectional study conducted on 73 psoriasis patients, Coimbra *et al.* noted that CRP serum levels were related to PASI scores and that they could be reduced by using NB-UVB as a treatment. Consequently, it is suggested that CRP serum levels can be considered a useful marker for diagnosing psoriasis severity and monitoring disease activity or the disease's reaction to treatment.[10]

In another study of 175 male psoriasis patients performed by Chodorowska, the clinical activity of psoriasis was calculated based on the PASI score, which reflected the increase in CRP serum levels during the acute phase (P<0.001).[11]

Strober *et al.* investigated the etanercept effects on CRP serum levels and observed increased CRP serum levels in patients with moderate to severe plaque-type psoriasis who were suffering from systemic inflammation. The activity of the skin disease was accompanied closely by improvement in serum CRP levels.[12]

Kanelleas *et al.* analyzed the role of inflammatory markers among psoriasis patients to evaluate the severity of the disease and its response to treatment. Furthermore, they found that inflammatory markers such as CRP serum levels diminish post-treatment (P<0.001) and identified a relationship between PASI scores and CRP. Due to this relation, inflammatory markers, especially CRP,

can be used to evaluate the severity of psoriasis and its response to treatment. In addition, the inflammatory markers, together with the PASI score, may represent an inflammatory situation for psoriasis.[13]

CONCLUSION

According to the data recorded in the literature and the current survey results, the augmented CRP serum levels were found in patients with moderate to severe plaque-type psoriasis, marking the systemic inflammatory feature of this disease. We gathered evidence that correlates psoriasis severity with CRP. The study suggested that CRP serum levels increase with psoriasis disease activity, which is measured by the PASI score. Moreover, it was shown that using NBUVB 311nm phototherapy not only improves psoriasis lesions, but also reduces CRP serum levels. The aforementioned findings were supported by statistical evaluations on the relationship between serum CRP levels, PASI scores and clinical observations. It is noticeable that CRP levels are generally likely to decrease with the reduction of disease severity, due to the different treatment modalities, including phototherapy. On this topic, we would recommend that future studies compare the effects of various treatment modalities on CRP levels in psoriatic patients.❑

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