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Trend of C-Reactive Protein and Erythrocyte Sedimentation Rates in Psoriatic Patients on Treatment of Standard Protocol of Infliximab

Abbas Zamanian[1], Amir Houshang Ehsani[2], Seyyedeh Bahareh Darvari[1]✉, Golnaz Mehran[1], Arghavan Azizpour[2]

[1] Rasoul-e-Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
[2] Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: Psoriasis is a chronic and inflammatory dermatologic disease. Inflammatory biomarkers such as C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) are known as immediate and delayed inflammatory biomarkers, respectively. Due to the fact that anti-inflammatory drugs such as Infliximab are widely used in psoriasis treatment, the aim of this study was to evaluate ESR, CRP and PASI scores in patients treated with Infliximab in a 24 week trend. **Materials and Methods:** This study was accomplished as a before-after study. Twenty seven psoriatic patients were included and standard Infliximab therapy was applied. All patients underwent 3 times of blood collection and in each session CRP, ESR and PASI scores were measured at the beginning of study and at the 12th and 24th weeks of follow-up **Results:** A total of 19 (70.4%) men and 8 (29.6%) women were evaluated. Mean age was 37.85±13.68 years. All three parameters had significant decrease in treatment course ($p<0.001$); however, no significant correlation was found between PASI and inflammatory biomarkers. Trends of ESR and CRP were significantly correlated in all patients ($r=0.504$, $P=0.007$) and males ($r=0.739$, $P=0.036$). **Conclusion:** Our study demonstrated that CRP and ESR decreased in Infliximab treatment, in accordance but non-regarded to PASI score decease. Regarding other studies results, using these biomarkers for treatment follow-up might need more caution. **[GMJ. 2015;4(1):8-13]**

Keywords: C-reactive Protein; Erythrocyte Sedimentation Rate; Psoriasis; Infliximab

Introduction

Psoriasis is a chronic and recurrent dermatologic disease, which despite several treatment protocols, there is no definite cure [1]. Etiology of this disease consists of epidermal growth and differentiation disturbance, and biochemical, immunological and vascular disorders. It affects both sexes equally and its prevalence ranges from 0.1% to 11.8% in different populations [2-4]. Several types of psoriasis have been demonstrated, and therefore, different types of treatment have been proposed [5].

Furthermore, psoriasis can affect patients' quality of life by altering social and psycho-

GMJ

Fax: +98 731 2227091
PO Box 7461686688
Email:info@gmj.ir

✉ **Correspondence to:**
Seyyedeh Bahareh Darvari, Dermotology Resident in Rasoul-e-Akram Hospital, Iran University of Medical Sciences
Tel (Fax): (+98) 9124425563
Email Address: twee_t2007@yahoo.com

logical disorders regarding external appearance of victims, resulting in low self-esteem, stigma, sexual disorders and lack of educational abilities [6]. The disease self-limiting period can be as short as a few months till long as decades and only occurs in nearly half of the patients [7]. Therefore, treatment and treatment follow-up are among the most important factors in supervising these patients. Regarding the fact that psoriasis is a chronic and maybe life-lasting disease, there should be a follow-up system and medications should be as harmless as possible; noting that insight to their conditions is a very important issue in treating the patients [8].

Anti-Tumor nercoting factor type alpha (TNF-α) drugs are widely used in immunologic and rheumatic diseases such as rheumatoid arthritis and psoriasis. TNF-α is a type of cytokine produced by immune system in rheumatic diseases. This biochemical marker reduces when immunologic response and inflammation decrease resulting by treatment of anti-TNF-α drugs such as Infliximab of disease self-limitation period. On the other hand, other inflammatory biomarkers such as C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) are known as immediate and delayed inflammatory biomarkers, respectively. Therefore, it is completely logical to conclude, perhaps ESR and CRP can be used as available, easy to interpret and cost-benefit tests in patients with psoriasis, treated with anti- TNF-α drugs [9-10]. Given that Infliximab is one of the most prevalent anti-TNF-α drugs used in our clinics, the aim of this study was to evaluate the trend of ESR and CRP in patients with psoriasis, under treatment of standard protocol of Infliximab regarding the severity of their disease.

Materials and Methods

Design and Subjects

This study was conducted as a before-after study at two dermatology referral centers of Tehran University of Medical Sciences affiliated hospitals; Razi and Rasoul-Akram. Sampling in our study was based on convenient method and all available patients were entered who had our eligibility criterion during a one-year period from January 2013. Sample size was based on Altman Nomogram with α=0.05 and β=0.2. Our inclusion criteria contained net diagnosis of Psoriasis, necessity of treatment with anti TNF-α (Infliximab) in moderate to severe forms of the disease and absence of any limitations to prescribe e.g. hypersensitivity reactions. Pregnancy or lactation, simultaneous usage of other anti-cytotoxic drugs and the presence of any intolerable side effects during treatment period were considered as other exclusion criteria. Of all entered patients, those who were not cooperative or accessible for follow-up, those with hematologic changes or activation of latent infections were also excluded. During treatment period, the presence of any new onset of the disease or deterioration of symptoms made it necessary to change our approach. Furthermore, patients with known thyroid dysfunction and hepatic or kidney failure were excluded from our study at any point of the research.

Demographic characteristics were entered to a self-designed checklist. Patients were selected to receive intravenous Infliximab 5 mg/kg according to the stage of disease and clinical assessment. Treatment was followed by the same dosage after two and six weeks of the initial infusion and then applied every eight weeks to 48 weeks. To assess clinical improvement according to Psoriasis Area and Severity Index (PASI) score, patients were advised to refer to our dermatologist within the next 12 and 24 weeks. At the initiation of the study and within further defined intervals, patients' ESR and CRP were checked parallel to their clinical assessment. Attained results at the first session were compared with further findings. Also the relation between clinical scores and changes in laboratory markers was investigated.

Biochemical Assessments

All patients underwent 3 times of blood collection and in each session, CRP, ESR and PASI were measured. All blood collections were performed at 12 PM from antecubital veins. All biochemical assays were carried out in Institute of Endocrine and Metabolism laboratory. CRP levels were measured with high sensitive CRP (hs-CRP) assay based on the principle of a solid phase enzyme-linked immunosorbent assay (ELISA) using goat an-

ti-human CRP antibody (hs-CRP ELISA kit, DRG Instrument GmbH, Germany). Intra- and inter-assay coefficients of variation (CV) are both under 5%. ESR was measured by anti-coagulated blood, using sodium citrate anti-coagulan, placed in an upright Westergren tube, and the rate at which the red blood cells fall, was measured and reported in mm/h.
Furthermore, for calculating PASI score, body was divided into four sections (head (H) (10% of a person's skin); arms (A) (20%); trunk (T) (30%); legs (L) (40%)). Each of these areas is scored by itself, and then four scores are combined into final PASI.

Statistics Analysis
Data were fed into SPSS software version 18 for analysis. To present demographic data, descriptive analysis was applied. Quantitative variables were demonstrated by mean±SD and qualitative variable with numbers and percentages. To compare achieved laboratory results before and after a special time, we used paired T-test. Repeated measure ANOVA was used to check the progression of disease or repeated laboratory findings in the course of time. The significance level was considered less than 0.05.

Ethical Approval
This study was conducted by the research institutional review board of Tehran University of Medical sciences (TUMS). During the study, ethical aspects and the progression of study were followed by the review board of the affiliated hospitals. All researchers involved in this study respected Helsinki's declaration ethical codes. Patients were convinced about the aim of the study and a written consent was signed prior to study. Financial supports were provided by the university and authors did not have any conflict of interest.

Results

A total number of 27 patients were evaluated, consisting of 19 (70.4%) men and 8 (29.6%) women. Mean age was 37.85±13.68 year-without any significant difference between genders. All patients were evaluated for liver, thyroid and kidney functions, which all results relied on normal range; therefore, none of the patients were excluded.
All patients underwent 3 times of CRP, ESR and PASI measurements. As seen in table 1, all three parameters had significant decrease in the treatment course ($p<0.001$), however, no significant correlation was fount between PASI and inflammatory biomarkers.
For further analysis, ESR and CRP trends were evaluated in each gender. As seen in table 3, the trends of ESR and CRP were sig-

Table 1. Three times of CRP, ESR and PASI measurements, all three parameters had significant decrease in the treatment course. No significant difference was seen between males and females. (*: tMann-Whitney-U test, ł: repeated measurement test)

		Total	Male	Female	P value*
PASI	First	22.95	21.67	25.65	0.307
	Second	10.25	9.65	11.67	0.349
	Third	6.39	5.76	7.41	0.345
pł		<0.001	<0.001	<0.001	
CRP	First	8.1	8.76	6.55	0.350
	Second	5.46	6.14	4.46	0.421
	Third	3.37	4.51	3.02	0.712
pł		<0.001	<0.001	<0.001	
ESR	First	21.93	23.74	17.62	0.481
	Second	15.04	16.11	12.5	0.258
	Third	12.56	13.37	10. 62	0.438
pł		<0.001	<0.001	<0.001	

Table 2. Correlation test between PASI score and inflammatory biomarkers; no significant correlation was detected

		CRP	ESR
Correlation	PASI 1	r=0.087, P =0.862	r=0.068, P =0.738
	PASI 2	r=0.097, P =0.629	r=0.113, P =0.573
	PASI 3	r=0.199, P =320	r=0.191, P =0.340

Table 3. Changes in PASI, CRP and ESR between first and last measurements. Significant correlation was found between ESR and CRP in total patient and male subjects

	Total	Male	Female
ΔPASI (1)	16.45±8.30	15.81±8.30	18.23±8.57
ΔCRP (2)	4.73±3.57	5.24±3.75	3.51±2.98
ΔESR (3)	9.37±10.07	10.36±8.00	7.00±14.25
(1) and (2)	r=0.144, P =0.472	r=0.553, P =0.156	r=0.066, P =0.788
(1) and (3)	r=0.113, P =0.576	r=0.011, P =0.979	r=0.237, P =0.329
(2) and (3)	r=0.504, P =0.007	r=0.739, P =0.036	r=0.406, P =0.085

nificantly correlated in total patients (r=0.504, P=0.007) and men (r=0.739, P=0.036).

Discussion

The aim of this study was to evaluate ESR, CRP and PASI scores in patients treated with Infliximab in a 24-week trend. In spite of significant changes in all 3 parameters, mean change of PASI score was not correlated with our inflammatory biomarkers. This means changing pattern of CRP and ESR are different from psoriasis severity.

Psoriasis is a chronic and hyper-proliferative disorder with dermatologic and systemic symptoms. Efforts have been made to demonstrate a new inflammatory-based biomarker for evaluating the treatment process; however, PASI score is still the best option. There are studies evaluating these biomarkers, especially CRP because it has limited half-life, sensitive tests used to evaluate other risk factors such as cardiovascular diseases [1-12].

There are not so many studies regarding CRP and psoriasis severity in the literature, most of which demonstrate that there are some relations between CRP and PASI scores. However, none of the studies have introduced a validated categorization or cut-off point and all of them have only demonstrated a significant increase of CRP in rheumatologic flare-up. For example, Arias-Santiago et al. [13] have compared 72 plaque psoriases with normal subjects and concluded that PASI correlate with CRP. Furthermore, Nisa et al. [14] reported the same results in150 diffuse psoriasis. However, our study demonstrated that both CRP and PASI scores decrease during treatment, no significant correlation was found; maybe due to multiple types of psoriasis, lower sample size or lack of other influential factors analysis. In accordance with our study, Kanelleas et al. [15] and Citrad et al. [16] did not find any significant correlation among inflammatory biomarkers and PASI scores in plaque psoriasis. Controversies are higher in interpreting ESR Blackmore et al. [17] and Salvarani et al. [18] which have demonstrated a weak correlation between ESR and PASI scores evaluated mainly in Psoriatic Arthritis. It seems that regarding psoriasis patients' follow-up CRP and ESR should be considered with extreme caution due to lack of strong evidence. However, US guidelines have suggested CRP for non-arthritis and ESR for arthritis psoriasis patients' follow-up [19].

All of these studies have demonstrated that CRP has reduced significantly; however, in studies with longer follow-ups, CRP never happened to reach the initial point or to normal baseline. Some studies demonstrated that this residual higher CRP can be a trigger for dis-

ease relapse; furthermore, immediate increase of CRP after the end of treatment shows that disease has not reached the remission phase [15-19]. Only in two trials on the relation between treatment and CRP, Strober et al. [20] demonstrated reduction of CRP with Etanercept (except arthritic psoriasis) and the other study showed that narrow band UVB even without significant change in PASI, decreased CRP in a significant way [21]. However, there are not enough studies regarding anti TNF-α drugs and CRP. Gisondi et al. and Lora et al. [22] both demonstrated reduced CRP, not in psoriasis, by Infliximab. However, other drugs such as Cyclosporine, Methotrexate and Psoralen were assessed and all of them were strong independent reducers of CRP in different studies. Likewise, Salvarani et al. [18], Castro et al. [23] and Heinberg et al. [21] have documented reduced ESR regarding Infliximab therapy in different diseases; though with longer follow-ups. Fortunately, our study was long enough to demonstrate reduction of both ESR and CRP.

We should note that even in accordance with nearly all studies in this regard, there is no study demonstrating mid-term or long-term relation between inflammatory markers and psoriasis. Questions such as "Is CRP residue related to disease flare-up?" or "do patients with higher CRP disease are influenced by other risk factors?" are still unanswered. Furthermore, our study suffered from two major limitations: 1- the number of patients who met our criteria and willingly entered the study were very low, so we could not evaluate the result for a large sample size; 2- there was no CRP baseline for patients before the first flare-up of the disease limiting our results and reduced the power of our study comparing normal patients.

Conclusion

Patients with moderate to severe forms of psoriasis have higher CRP and ESR compared to normal subjects. Our study demonstrated that CRP and ESR decreased in Infliximab treatment, in accordance but non-regarded to the PASI score decease. Using these biomarkers for treatment follow-up might need more caution.

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Conflicts of Interest

None declared.

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