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Evaluation of neopterin level and disease severity in patients with psoriasis vulgaris treated with narrowband UVB

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Abstract

Background: Neopterin is a biochemical marker of cellular immunity. It has been reported that serum and urine neopterin levels increase in psoriasis and decrease with treatment. Nevertheless, assessment of a direct link between narrowband ultraviolet B (UVB) therapy and neopterin level in association with Psoriasis Area and Severity Index (PASI) scores has not been performed yet. We aimed to evaluate the serum neopterin level in patients with psoriasis treated with narrowband UVB therapy in association with disease severity. **Materials and Methods:** The study included 35 patients with chronic plaque-type psoriasis who had PASI scores of >10 or below 10 but resistant to topical therapies and 30 healthy individuals. The narrowband UVB therapy was administered to the patient group (n = 35). Serum neopterin analysis was performed with an enzyme-linked immunosorbent assay method before and after treatment. **Results:** There was statistically significant correlation between neopterin level and PASI score in the patient group (P = 0.011). The serum neopterin level was significantly increased in patients with higher PASI score. Moreover, the serum neopterin level was found to be statistically higher in severe psoriasis group (PASI score ≥10, n = 14) than the mild-moderate group (PASI score <10, n = 21) (P = 0.001). Furthermore, a significant decrease was observed according to serum neopterin level after the narrowband UVB therapy in the remaining 20 patients who were able to comply with the scheduled therapy and follow-up procedure (P = 0.026). **Conclusion:** Serum neopterin levels were found to be an useful marker for evaluating disease severity and efficacy of narrowband UVB treatment. Thus, our findings may provide a new approach with the management of disease and follow-up strategies in patients with psoriasis.

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Full Text

Introduction

Psoriasis is a widespread immune-mediated, inflammatory disease with unknown etiology affecting approximately 3% of the population.[1] It is characterized by well-defined, erythematous and scaly plaques typically located on the scalp, knee, or elbow.[1] Psoriasis and its linked systemic comorbidities have also a major impact particularly on health-related quality of life.[2] The underlying pathogenesis of the lesions is associated with elevated production of tumor necrosis factor-α, inflammation, keratinocyte proliferation and differentiation, and vascular changes.[3]

The diagnosis of the disease is mainly dependent on clinical examination; there is no complete cure for psoriasis yet. Treatment is mainly focused on period of remission or decreasing the severity with topical, systemic, and ultraviolet light–based therapies as well as several new treatment options such as biological drugs.[4] Although there are some concerns about skin cancer risk, narrowband ultraviolet B (UVB) phototherapy is found to be safe and effective in clinical trials; moreover, it is associated with improved quality of life assessments in patients diagnosed with psoriasis.[5],[6]

Neopterin is a nonspecific indicator of cellular immunity, excreted from macrophages and monocytes upon stimulation with interferon-γ which is released from active T helper-1 (Th1) cells.[7] Increased levels of neopterin within serum and urine were associated with psoriasis in published data. Furthermore, significant correlation between neopterin level and Psoriasis Area and Severity Index (PASI) score, in addition to decreasing neopterin level after topical and systematic therapies, was documented as well.[8],[9],[10] Nevertheless assessment of a direct link between narrowband UVB therapy and neopterin levels in association with PASI scores has not been reported yet.

Therefore, we aimed to evaluate the serum neopterin level in patients with psoriasis treated with narrowband UVB therapy in association with disease severity.

Materials and Methods

This study was performed with the Institutional Review Board protocol approval, date 20.09.2013 and number 10/22 in Dıskapı Research and Training Hospital, Department of Dermatology between September 2013 and December 2013. This single-centered, prospective-controlled study included 35 patients between 18 and 65 years of age, who were clinically and histopathologically diagnosed with psoriasis vulgaris and had PASI scores >10 or below 10 but resistant to topical therapies. A parallel (by gender, age) healthy control group (n = 30) without family history of psoriasis was also included in our study. Patients with psoriatic arthritis, pustular psoriasis, palmoplantar psoriasis, active and chronic infections, obvious malignancies, systemic inflammatory and immunosuppressive disease, metabolic syndrome, and participants who were receiving any topical therapy within the last 2 weeks or systemic therapy within the last month were excluded from our study. In addition, participants were enrolled in the study after obtaining written informed consent.

The severity of the disease was assessed using PASI. Patients' demographic characteristics and the mean scores of PASI before and after treatment were recorded and documented in both the study groups. The narrowband UVB therapy was administered to patients who had PASI scores >10 or below 10 but resistant to topical therapies. Fifteen patients who were unable to comply with the scheduled therapy and follow-up procedure were excluded from the study. Thus, pre- and posttreatment procedures were performed only with 20 patients.

The serum neopterin analysis was performed with an enzyme-linked immunosorbent assay (ELISA; Instruments GmbH, Germany) method at a normality level of 0.3–3.0 ng/mL.

Statistical analysis

All the data were analyzed using SPSS (Statistical Package for the Social Sciences) software for Windows (v21.0; IBM, Armonk, NY, USA). Individual and aggregate data were summarized using descriptive statistics including mean, standart deviations, median (min–max), frequency distribution, and percentage. Normality of data distribution was verified by Kolmogorov–Smirnov test. Evaluation of categorical variables was performed by Chi-square test (Fisher's exact test). For variables that were not normally distributed, Mann–Whitney and Kruskal–Wallis tests were conducted to compare between groups. We used Spearman's test to examine correlation between PASI scores and neopterin levels. P values of <0.05 were considered statistically significant.

Results

Patients diagnosed with psoriasis (n = 35) in this study were 12 (34.3%) male and 23 (65.7%) female, and the mean age of 35 patients was 38.40 ± 12.39 years. In addition, 19 (63.3%) of the control group were female and 11 (36.7%) were male. The mean age of the control group was 36.73 ± 12.93 years [Table 1]. There were no statistically significant differences in the age and gender between the two groups (P > 0.05).{Table 1}

The mean score of PASI was 9.92 ± 4.52 (range = 3–30.2) in the patient group. In addition, the mean level of initial serum neopterin was 1.62 ± 1.30 ng/ml in the patient group and 1.29 ± 1.32 ng/ml in the control group. No statistically significant difference was found according to the serum neopterin levels between groups (P = 0.378) [Table 1]. There was positive moderate statistically significant correlation detected between serum neopterin levels and PASI scores in patients with psoriasis (P = 0.011; r = +0.423).

Patients with psoriasis were divided into two groups according to the severity of the disease: severe psoriasis (PASI score ≥10) and mild-moderate psoriasis (PASI score <10). The severe psoriasis group consisted of 14 (40%) patients and the mild-moderate psoriasis group consisted of 21 (60%) patients. The mean serum neopterin level was 1.19 ± 0.18 ng/ml in the mild-moderate psoriasis group and 2.26 ± 1.92 ng/ml in the severe psoriasis group. Thus, serum neopterin levels were found to be statistically higher in the severe psoriasis group than in the mild-moderate psoriasis group (P = 0.001).

Fifteen patients who were unable to comply with the scheduled therapy and follow-up procedure were excluded from further analysis. Therefore, pre- and posttreatment procedures were performed with 20 patients. The pretreatment serum neopterin level was 1.57 ± 0.77 ng/ml and it was 1.20 ± 0.25 ng/ml after therapy in the remaining 20 patients. Thus, a statistically significant decrease in serum neopterin level was observed in the remaining 20 patients after narrowband UVB therapy (P = 0.026).

Discussion

Psoriasis is a chronic inflammatory disease of the skin of unknown etiology.[1] This heterogeneous disease presents with typical erythematous and scaly plaques to many severe systemic involvement and comorbidities such as cardiovascular disease, psoriatic arthritis, and psychiatric disorders as well.[11] PASI is a gold standard assessment tool of disease severity.[12] Although guidelines recommend PASI of ≥10 as a threshold for initiating treatment in patients with moderate to severe psoriasis, the other factors such as response to topical therapies, gender, age, and comorbidities influence treatment decision.[13] Koç et al. reported a median PASI score of 13.2 (range: 3.3–32.4) in 22 patients with psoriasis in the pretreatment period in their study which aimed to investigate urine neopterin levels in patients with psoriasis.[14] A study by Ceyhan et al. documented a mean PASI score of 9.7 ± 6.1 in 40 patients with psoriasis.[15] Similarly, the mean score of PASI was 9.92 ± 4.52 (range: 3–30.2) in our patients (n = 35).

Phototherapies are well established and effective procedures in the treatment of psoriasis.[16] The narrowband UVB widely used external therapy which influences immune mechanisms by supressesing both T lymphocyte proliferation and Th1-type cytokine excretion.[17] Grundmann-Kollmann et al. obtained equal responses from narrowband UVB and PUVA therapy methods for psoriasis in their study.[16] Therefore, we used narrowband UVB therapy in our study. The narrowband UVB therapy was administered to our patients who had PASI scores >10 or below 10 but resistant to topical therapies.

A considerable amount of study highlighted the direct link between neopterin production and severity of inflammatory and autoimmune diseases. Thus, increased levels of neopterin in biological fluids were not only associated with psoriasis but also associated with disease activity in published data.[9],[14],[15] Koç et al. measured urine neopterin levels by high-performance liquid chromatography method in pre-/posttreatment period with etanercept in 22 patients. They reported significantly higher pretreatment levels of neopterin than the healthy control group, nonpsoriatic patient group with inflammatory skin diseases, and posttreatment patient group as well (P < 0.001). In addition, there was no statistically significant correlation observed between neopterin levels and PASI scores in their study.[14] Similarly, Ceyhan et al. reported a statistically higher (P < 0.001) serum levels of neopterin (11.04 ± 5.42 nmol/l) in 40 patients with psoriasis than in the control group (5.44 ± 2.40 nmol/L) and they found no significant correlation between neopterin level and PASI score.[15] Okubo et al. also documented a statistically higher serum level of neopterin than the control group, and also insignificant

correlation between neopterin level and PASI score.[18] On the other hand, Fuchs et al. noted a statistically significant decrease in serum and urine neopterin levels by cyclosporin A treatment; moreover, they reported a significant correlation between neopterin level and PASI score.[8] Supportively, Harland et al. reported significantly higher pretreatment level of urine neopterin than in the healthy control group, and they showed statistically significant decrease in urine neopterin level by UVB plus topical tar or dithranol or PUVA treatment in 40 patients with psoriasis; moreover, they reported a strongly significant correlation between neopterin level and PASI score ($P = 0.001$).[9] Sanchez-Regana et al. concluded that serum neopterin level might contribute as a marker for both disease activity and treatment efficacy in their study in which 24 patients with psoriasis were treated by triamcinolone acetonide 0.1% cream and coal tar 4%.[10] On the contrary, no statistically significant decrease was observed in neopterin level after cyclosporin A treatment in a study by Economidou et al.[19] Since a majority (60%) of our patients had mild-moderate psoriasis, this could explain the statistically insignificant findings for pretreatment neopterin level between patient and control groups. Supportively, serum neopterin level was found to be statistically higher in the severe psoriasis group than in the mild-moderate psoriasis group. Furthermore, a statistically significant decrease in serum neopterin level was observed after narrowband UVB therapy in 20 patients who were able to comply with the scheduled therapy and follow-up procedure.

Published data about neopterin level in biological fluids and its correlation with PASI score seem to be conflicting. Moreover, it is obvious that major variables that influence the results of researches are different treatment procedures. In addition, to our knowledge, no published data are available such as evaluation of serum neopterin levels in patients with psoriasis treated with only narrowband UVB therapy in association with disease severity. In this respect, considering that different treatment procedures result in different study results, serum neopterin level may be used as a useful marker for both disease severity and narrowband UVB treatment efficacy. Thus, our findings may provide a new approach with the management of disease activity and treatment efficacy follow-up strategies in patients with psoriasis. Further researches should be performed with larger study groups to achieve more assuring results.

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Conflicts of interest

There are no conflicts of interest.

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