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Research article

Impact of depressive symptoms on oxidative stress in patients with psoriasis

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Background: Depression and anxiety disorders often accompany psoriasis. Increased reactive oxygen radicals and impaired antioxidant systems are considered to play a role both in psoriasis and depression and anxiety disorders. Accordingly, in this study, we aimed to investigate the effects of depressive and anxiety symptoms on oxidative stress in patients with psoriasis.

Materials and methods: Hospital Anxiety and Depression Scale (HADS) forms were completed by 39 psoriasis patients and 25 volunteer controls. Serum total antioxidant capacity (TAC) and total oxidant capacity (TOC) parameters were analysed in serum samples, after which oxidative stress index (OSI) was calculated in whole study population. Laboratory data were analysed with a Kruskal–Wallis test to determine the severity of HADS and the presence of psoriasis among four groups.

Results: The psoriasis patients had higher HADS scores, higher OSI and TOC levels, and lower TAC levels compared with the control group. Comparison among four groups with/without psoriasis and higher/lower HADS scores revealed statistically significant differences with regard to TAC (Kruskal–Wallis $P = 0.0047$) and TOC (Kruskal–Wallis $P < 0.001$) levels and OSI (Kruskal–Wallis $P < 0.001$); the difference was mainly based on the difference between cases with and without psoriasis and on HADS scores in control subjects ($P < 0.05$ for *post hoc* comparisons). TAC, TOC, and OSI levels did not differ significantly in psoriasis patients with regard to higher or lower HADS scores.

Conclusion: Based on the findings of this study, the presence of either psoriasis or higher HADS scores in the control subjects was associated with increased oxidative stress, whereas presence of higher HADS scores did not lead to further increase in oxidative stress in psoriatic patients.

Keywords: Psoriasis disease, Depressive symptoms, Oxidative stress index

Introduction

Psoriasis is a chronic, inflammatory, autoimmune skin disorder with a prevalence of 1–3%. The clinical picture includes psoriatic squama on an erythematous ground, itchy papules and plaques, as well as dry skin, all of which have an impact on daily activities and social functions.[1] Recent studies suggest that psoriasis is not only limited to the skin and joints, but also affects the cardiovascular and gastrointestinal systems, the metabolism, the eyes, and psychiatric involvement.[2] Visible psoriatic lesions might cause a disruption in social relations (embarrassment) and a decrease in self-esteem, which can lead to many psychiatric problems, such as depression, anxiety, and suicidal ideation.[1,3]

Epidermal reactive oxygen radical (ROS) sources may be endogenous (such as radicals formed due to activated neutrophils or enzyme activities, such as NADPH oxidase, xanthine oxidase, lipoxygenase, and nitric oxide synthases) or exogenous (such as ultraviolet rays, which are pro-oxidative stimulants, atmospheric gases, microorganisms, pollution, and xenobiotics).[4,5] In healthy individuals, the ROS that is formed as a result of normal metabolism is removed by antioxidant defence mechanisms of the body, whereas increased oxidative stress takes place in cases of impaired oxidant/antioxidant balance that favour the oxidant side.[6–8]

Clinical scenarios of impaired oxidant/antioxidant balance characterized by an increase in ROS

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generation and compromised antioxidant system have recently been reported as playing a role in the pathogenesis of psoriasis disease.[9]

The brain generates large amounts of oxygen radicals with increased ROS production, as the brain is rich in lipid substrates for oxidation, as well as abundant iron and copper ions that catalyse free radical reactions and neurotransmitters that act as reducing agents, such as noradrenalin and dopamine.[10] Considering that the brain is relatively sensitive to oxidative damage, oxidative stress might play a role in the pathogenesis of many major psychiatric disorders, and an increase in neurotransmitter oxidation may be associated with lipid peroxidation and major depression as well.[11]

To date, the effects of depressive symptoms on the oxidative system have not been studied in psoriasis disease, although the effects of both psoriasis and psychiatric disorders on the oxidative system have been independently studied. Accordingly, we aimed to evaluate the effects of depressive symptoms on the oxidative system in psoriasis patients.

Materials and method

Subjects

The study included 39 patients (17 male and 22 female) with recent active psoriasis lesions and 25 healthy volunteers (10 male and 15 female) as a control group. The psoriasis patients and healthy volunteers met our inclusion criteria and agreed to participate in the study. The Hospital Anxiety and Depression Scale (HADS) was administered by a psychiatrist. Blood samples were obtained from the patient and control groups to measure total antioxidant capacity (TAC) and total oxidant capacity (TOC) parameters. The study protocol followed the Declaration of Helsinki; all subjects were informed about the study protocol, and written consent was obtained from all participants or their guardians. The study was approved by the local Clinical Research Ethics Committee.

Members of the study population were over 15 years old and at least primary school graduates. Exclusion criteria included the presence of chronic disease, concomitant inflammatory diseases such as infections and autoimmune disorders, immune-compromised state, diabetes mellitus, familial hypercholesterolemia, neoplastic diseases, liver or kidney diseases, and recent major surgical procedure. Subjects taking anti-psoriatic, antipsychotic, or antioxidant agents, vitamins, diuretics, or hormone replacement therapy, as well as smokers and those with alcoholism, were also excluded.

Hospital Anxiety and Depression Scale

The HADS was first developed by Zigmond and Snaith in 1983. It consists of 14 multiple-choice questions and provides two sub-scores (anxiety and depression) and a total score. The HADS is accepted as a reliable screening instrument for clinically significant anxiety and depression and has been found to be a valid measure of the severity of these disorders.[12–14] The HADS total score is also a valid measure of 'emotional distress' or 'psychological distress'; as such, the HADS can be used as a measure of overall psychiatric morbidity.[15] The validity and reliability of the Turkish version of HADS was demonstrated by Aydemir *et al.* in 1997. Using ROC analysis, a score of 7 was found to be the cut-off for the depression subscale, and a score of 10 for the anxiety subscale. As a result, the Turkish version of HADS is valid and reliable for assessing clinical depression or anxiety in medically ill patients.[16]

Measurement of total antioxidant capacity

TAC serum levels were determined using commercially available diagnostic kits (Rel Assay, Gaziantep, Turkey) with an auto-analyser (Aeroset®; Abbott, Abbott Park, IL, USA). Using this method, Fe^{+2}-o-dianisidine complex with hydrogen peroxide generates OH^{-} radicals by a Fenton-type reaction. This powerful, reduced ROS reacts with colourless o-dianisidine molecules in low pH to form yellow-brown dianisidine radicals. Dianisidine radicals increase the formation of the colour by participating in an advanced oxidation reaction.

However, antioxidants that stop these oxidation reactions suppress the formation of the colour. The results were provided by automated analysers used to measure this reaction spectrophotometrically at 240 nm. Trolox, a water-soluble vitamin E analogue, was used as a calibrator. The results are expressed as mmol Trolox.[17]

Measurement of total oxidant capacity

TOC serum levels were determined using commercially available diagnostic kits (Rel Assay) with an auto-analyser (Aeroset®). Oxidants oxidize the ferrous ion-o-dianisidine complex into ferric ion; glycerol present in the media accelerates this reaction three-fold. Ferric ions form a coloured complex with xylenol orange in acidic media. The intensity of the colour, which is related to the amount of oxidants in the sample, was measured spectrophotometrically. H_2O_2 was used as a standard, and the results were expressed as μmol H_2O_2 equivalent/L.[18]

Calculation of oxidative stress index

The ratio of TOC to TAC gave the oxidative stress index (OSI), an indicator of the degree of oxidative stress. To perform the calculation, the TOC, expressed as mmol Trolox equivalent/L, was converted to μmol equivalent/L, and the OSI value was calculated by the

following formula: OSI (arbitrary unit) = TOC (μmol H_2O_2 equiv/L)/10 × TAC (mmol Trolox Equiv/L).[19]

Statistical analysis

All analyses were conducted using the SPSS statistical program (version 16.0 for Windows; SPSS, Chicago, IL, USA). The distribution of continuous variables was evaluated with a one-sample Kolmogorov–Smirnov test. Comparisons of the categorical variables between the patients and controls were performed with χ^2 and Fisher's exact tests, and Student's *t* tests and Mann–Whitney *U* tests were used to compare the continuous variables. A Kruskal–Wallis test was used for comparisons of the four groups (Group 1: Psoriatic patients with high depression scores; Group 2: Psoriatic patients with low depression scores; Group 3: Healthy volunteers with high depression scores; Group 4: Healthy volunteers with low depression scores). Results for continuous variables were expressed as mean ± standard deviation, whereas categorical variables were expressed as either count or percentage. All statistical tests were two-sided, and a *P* value of <0.05 was considered statistically significant.

Results

Of the 39 psoriasis vulgaris patients, 17 were male and 22 were female; the mean age of the patient group was 28 ± 7 years (range: 18–47 years). The control group of 25 subjects was composed of 10 males and 15 females; their mean age was 28 ± 7 years (range: 16–50 years).

The mean total HADS score (15.97 ± 7.06 vs. 11.28 ± 6.25; $P = 0.021$) and mean depression score (8.18 ± 4.22 vs. 5.32 ± 3.85; $P = 0.008$) were significantly higher in the psoriasis patients compared with the controls, although the mean anxiety scores were similar between the two groups (7.79 ± 3.18 vs. 6.48 ± 3.03; $P = 0.105$). Mean total HADS, depression, and anxiety scores, respectively, were 19.65 ± 4.6, 10.35 ± 2.80, and 9.29 ±2.34 in the depressed group; 8.40 ± 3.57, 3.33 ± 1.99, and 5.00 ± 2.32 in the non-depressed group; 22.71 ± 3.76, 11.47 ± 2.76, and 11.24 ±1.20 in the anxious group; and 11.36 ± 5.24, 5.47 ± 3.57, and 5.85 ± 2.31 in the non-anxious group. The number of subjects with higher depression scores was significantly greater in the psoriasis group than in the controls ($P = 0.028$), although the anxiety scores were similar between the groups ($P = 0.126$) (Table 1).

Table 1 Comparison between patient and control groups in terms of depression, anxiety, TAC and TOC levels, and OSI values

	Patients (*n* = 39)	Controls (*n* = 25)	*P* value
High depression score (*n*)	25/39	9/25	0.028
High anxiety score (*n*)	13/39	4/25	0.126
TAC (mmol Trolox)	1.03 ± 0.19	1.19 ± 0.26	0.005
TOC (μmol H_2O_2 equivalent/L)	26.92 ± 7.82	17.75 ± 6.85	0.001
OSI (arbitrary units)	2.69 ± 0.89	1.60 ± 1.04	0.001

Serum TOC ($P = 0.001$) and OSI ($P = 0.001$) were statistically significantly higher and serum TAC ($P = 0.005$) was statistically significantly lower in the patient group compared with the control group (Table 1). Comparison of the four groups with regard to TAC ($P = 0.0047$), TOC ($P < 0.001$), and OSI ($P < 0.001$) revealed statistically significant differences among the groups (Table 2). In two group comparisons, Groups 1 and 2 were similar with regard to TAC, TOC, and OSI ($P > 0.05$ for all), whereas both Groups 1 and 2 were significantly different from both Groups 3 and 4 with regard to TOC ($P < 0.05$ for all), and Groups 1, 2, and 3 were significantly different from Group 4 with regard to TAC and OSI ($P < 0.05$ for all), and Group 1 was significantly different from Group 3 with regard to OSI ($P < 0.05$) (Table 2).

Discussion

In this study, we aimed to evaluate the impact of depression on oxidative stress in psoriasis patients, and our findings revealed that (i) HADS depression scores were significantly higher in the psoriasis patients compared with the controls; (ii) TAC levels

Table 2 Comparison of the effects of depressive scores on TAC and TOC levels and OSI values in the patient and control groups

	Patient group with high depressive scores (*n* = 25)	Patient group with low depressive scores (*n* = 14)	Control group with high depressive scores (*n* = 9)	Control group with low depressive scores (*n* = 16)	*P* value
TAC (mmol Trolox)	1.04 ± 0.22	1.00 ± 0.15	1.05 ± 0.27	1.28 ± 0.23	0.0047*
TOC (μmol H_2O_2 equivalent/L)	27.04 ± 8.31	26.72 ± 7.17	19.16 ± 6.81	16.97 ± 6.97	<0.001**
OSI (arbitrary units)	2.68 ± 0.96	2.71 ± 0.80	2.06 ± 0.34	1.30 ± 0.71	<0.001***

*$P < 0.05$ for group 1 vs. group 4; group 2 vs. group 4; group 3 vs. group 4.
**$P < 0.05$ for group 1 vs. group 3; group 1 vs. group 4; group 2 vs. group 3; group 2 vs. group 4.
***P < 0.05 for group 1 vs. group 3; group 1 vs. group 4; group 2 vs. group 4; group 3 vs. group 4.

were significantly lower and TOC and OSI levels were significantly higher in the psoriasis patients compared with the controls; and (iii) TAC, TOC, and OSI levels did not differ significantly among psoriasis patients with regard to the presence of high/low depression scores, although TAC and OSI levels were significantly different among the controls with regard to the presence of high/low depression scores.

Increased ROS levels were reported, as well as an inadequacy of the enzymatic and non-enzymatic antioxidant mechanisms, in the plasma and red blood cells of the psoriasis patients.[6,20,21] Furthermore, it was detected that a high number of pro-oxidative products were also secreted by leucocytes in the skin of the psoriasis patients;[22] these products especially affect keratinocytes and fibroblast cells.[23] Accordingly, there is an imbalance in the oxidant–antioxidant system in psoriasis patients, and increased ROS levels might play a role in the pathogenesis of this disease.[21,22,24,25]

Both Gabr and Al-Ghadir[21] and Hashemi *et al.*[25] have reported low TAC values in psoriasis patients compared with control groups. A decrease in serum antioxidants accompanied by an increase in serum oxidant levels has been reported in psoriasis patients, as well.[23,26] In our study, the patient group had lower serum TAC levels and higher serum TOC levels, as well as higher OSI values, compared with the control group. On the basis of these results, we can surmise that a compromised antioxidant defence mechanism, accompanied by increased oxidant levels and OSI values in psoriasis patients, might play an important role in the pathogenesis of this disease.

Various psychiatric complaints of depression and anxiety disorders are frequently seen in psoriasis patients.[27,28] Han *et al.*[29] reported depression in 9.2% of psoriasis patients and anxiety in 6.9%; in addition, several studies in the literature have revealed high rates of depression and anxiety in psoriasis patients.[30–37] Concordant with the literature, the frequency of high depressive scores was significantly greater in the psoriasis patients than in the controls in our study. However, contrary to the literature, the frequency of high anxiety scores was not significantly different between the two groups, which can mainly be explained by the limited sample size of our study.

Oxidative stress may have an impact on the pathogenesis of various psychiatric disorders. There are studies suggesting that ROS play an important role in the pathophysiology of depression and cause damage in neurons.[38,39] Functional loss and cell death have been observed in terms of neuron activity, development, and signal transmission under the effect of free radicals in the nervous system.[39,40] It is considered that there may be a significant relationship between the balance of oxidant and antioxidant defence and depressive symptoms.[11,41–43]

The relationship between psoriasis disease and depression might not only be explained by psychopathological reasons, as biological factors might also help to explain this relationship.[44] In our study, there were no differences in serum TAC and TOC levels or OSI values between the psoriasis patients with high depression scores and those with low depression scores; however, serum TAC and TOC levels and OSI values were higher in the psoriasis patients compared with the controls, both with high and low depression scores. The absence of statistically significant differences in serum TAC and TOC levels and OSI values between the psoriasis patients with high and low depression scores might be explained by the fact that oxidative stress plays a crucial role in psoriasis, and psoriasis patients already have elevated oxidative stress, which would not further reveal the impact of depression. As another explanation, we used HADS depression scores rather than clinical depression, and the presence of clinical depression would more greatly influence oxidative stress in psoriasis patients. Further large-scale prospective studies might better elucidate the impact of depression on oxidative stress in psoriasis patients.

In conclusion, HADS depression scores and oxidative stress are higher in psoriasis patients than in controls. TOC levels and OSI values are higher and TAC levels are lower in both psoriasis patients and controls with high depression scores, signifying the association of oxidative stress with both psoriasis and depression. The impact of concurrent psoriasis and clinical depression on oxidative stress remains to be established in further studies.

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