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Evaluation of Serum Homocysteine Levels in Patients with Cutaneous-Oral Lichen Planus and Psoriasis Patients

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Abstract

Background: An elevated plasma homocysteine level is suggested to be a risk factor for reversible atherosclerotic cardiovascular disease. Psoriasis and lichen planus are two chronic inflammatory skin diseases associated with an increased risk of thrombosis and cardiovascular disease. **Materials and Methods:** We conducted this descriptive analytical study in 2015 on 30 psoriatic patients and 30 patients with cutaneous-oral lichen planus (selected via a simple randomized method) who were referred to the outpatient department of dermatology at Bouali Sina training and therapeutic hospital in Sari, Iran. We evaluated the serum homocysteine, vitamin B12, and folic acid levels in all patients. Data were evaluated using descriptive statistics and an independent t-test. Logistic regression was used for controlling confounding variables. **Results:** Nine (30%) patients in the psoriasis group and 11 (36.66%) in the cutaneous-oral lichen planus group had abnormally high blood homocysteine level ($P = 0.001$). Serum vitamin B12 level in the psoriatic group was significantly higher than in the cutaneous-oral lichen planus group ($P = 0.034$). Both mean and maximum serum folic acid levels in the psoriatic group were higher than in the cutaneous-oral lichen planus group, but the difference was not significant ($P = 0.296$). As psoriasis and cutaneous-oral lichen planus are chronic inflammatory skin diseases, in these groups, the serum homocysteine levels were higher than in healthy control subjects, but there was no significant differences between the two groups. **Conclusion:** Further studies are recommended about the course of treatment in patients with psoriasis and lichen planus diseases before therapeutic intervention. [GMJ.2017;6(3):226-32] DOI: 10.22086/gmj.v0i0.749

Keywords: Homocysteine; Cutaneous Lichen Planus; Oral Lichen Planus; Psoriasis

Introduction

Chronic inflammation plays an important role in the development of cardiovascular risk factors [1]. In addition, several studies

have demonstrated the relationship between cardiovascular risk factors and dermatologic diseases, such as androgenetic alopecia, lichen planus and acne rosacea [2-5]. It has also been shown that psoriasis (a chronic



inflammatory skin condition) is associated with lower levels of folate and conversely higher levels of homocysteine, which is a risk factor for cardiovascular disease [6]. Another study showed that oral lichen planus (OLP), as a chronic immunologic mucocutaneous inflammatory oral mucosal disease, was associated with deficiencies of hemoglobin (Hb), iron, folic acid and vitamin B12 as well as increased blood homocysteine level [7]. Homocysteine is a sulfur-containing amino acid. It is a metabolite of methionine, another amino acid that is found in foods and transformed into homocysteine in the bloodstream. Vitamins B6 (pyridoxine), B12 and folate are essential cofactors in homocysteine metabolism. Being recycled back into methionine or converted to cysteine in the body are the two major metabolic pathways that lead to reduced homocysteine blood levels [8, 9]. There are several factors that may lead to hyperhomocysteinemia, such as high methionine diets, vitamin (vitamin B12 and B6, folic acid) deficiencies, male gender, increased age, renal dysfunction and genetic abnormalities [8, 9]. Hyperhomocysteinemia (>15 $\mu\text{mol/L}$) is also an independent cardiovascular risk factor that has been associated with atherosclerotic vascular diseases and ischemic heart attacks by a number of mechanisms of action, such as endothelial damage, promoting clot formation, decreasing the flexibility of blood vessels and reducing blood flow velocity. Homocysteine also increases levels of asymmetric dimethylarginine (ADMA), which is a natural inhibitor of nitric oxide (NO) synthase, which may increase production of superoxide. The oxidative reaction between superoxide and NO generates peroxynitrite and reduces NO which leading to endothelial dysfunction [6, 8, 10]. Several studies revealed an association between chronic inflammatory skin diseases and an increased risk of cardiovascular diseases, but unfortunately, no previous studies in this field have been published in Iran. So, this study was aimed to evaluate and compare the serum homocysteine, vitamin B12 and folic acid levels in patients with cutaneous-oral lichen planus and psoriasis patients.

Materials and Methods

This descriptive analytical study was conducted in 2015 on 30 psoriatic patients and 30 patients with cutaneous-oral lichen planus (selected via a simple randomized method) who were referred to the outpatient department of dermatology at Bouali Sina Hospital in Sari, Iran. The sample size was calculated based on a similar study [20]. Informed consent was obtained from all participants. Patients with anemia (Hb levels <14 $\mu\text{m/dl}$ in men and <12 $\mu\text{m/dl}$ in women); those using sulfur, folate or iron-containing drugs or supplements; those with a history of special disease (like cancer) and those who did not wish to voluntarily participate in the study were excluded. All participants were diagnosed by a dermatologist on the basis of characteristic clinical features and laboratory findings. Demographic characteristics such as sex, age and education levels were recorded. Venous blood samples were drawn from all participants after 12 hours fasting to determine serum Hb, vitamin B12, folic acid and homocysteine concentrations. To obtain serum, blood samples were centrifuged at 3000 rpm/min for 10 min. Then, serum samples were stored at -70 $^{\circ}\text{C}$ prior to analysis. Serum homocysteine levels were evaluated using a high-performance liquid-chromatography-based commercial kit. Vitamin B12 and folic acid levels were also measured by chemiluminescence immunoassay microparticle method.

Ethical Considerations

Ethical approval was obtained from the research ethics committee of the research deputy of the associated university of medical sciences. All the participants received oral and written information about the aims of the study. It was made clear to them that their participation was voluntary and that all data would remain confidential. Research participants could not be personally identified, and they were assured that participation would in no way affect their academic results.

Data Analysis

Collected data were analyzed using the

SPSS software package, version 20. Data were evaluated using descriptive statistics (mean, SD). An independent t-test was used to compare homocysteine levels in the two groups, and a cutoff of >15.3 mmol for men and >11.6 mmol for women was considered as abnormal serum homocysteine levels. Logistic regression was used for controlling confounding variables. Results were considered statistically significant at $P < 0.05$.

Results

Demographic characteristics, including the age and sex, of the patients in both the psoriasis and cutaneous-oral lichen planus groups are shown in (Table-1). Of the 60 patients, 30

patients were in the psoriasis group (8 (26.7%) men and 22 (73.3) women) and 30 patients (11 (38.7%) men and 19 (61.3%) women) were in cutaneous-oral lichen planus group. Sex distribution patterns were similar between the two groups ($P = 0.316$). In the psoriatic group, the age ranged from 20 to 72 years (with a mean of 41.63 ± 2.69 years), and in the cutaneous-oral lichen planus group, it ranged from 16 to 65 years (with a mean of 38 ± 2.62 years). There was no significant difference in age distribution pattern between the two groups ($P = 0.313$). However, there was a significant relationship between increasing age and elevated serum homocysteine levels, as blood homocysteine level increases 4.5% more than normal with each year of age ($P = 0.038$).

Table 1. Demographic Characteristics of the Patients in the Psoriatic and Cutaneous-Oral Lichen Planus Groups

Variables	Psoriasis	Cutaneous-oral lichen planus	P-value
Age*	41.63 ± 2.69	38 ± 2.62	0.313
Sex**			
Female	22 (73.3%)	19 (61.3%)	0.316
Male	8 (26.7%)	11 (38.7%)	
Education level**			
Literate or diploma	18 (60%)	13 (45.2%)	0.432
Bachelor's degree	6 (20%)	10 (33.3%)	
MSc or PhD	6 (20%)	7 (22.5%)	

*Presented as Mean ± SD, ** Presented as n(%), **MSc**: Master of Science

Table 2. Comparison of the Levels of Biochemical Variables in the Psoriatic and Cutaneous-Oral Lichen Planus Groups

Variables	Psoriasis	Cutaneous-oral lichen planus	P-value
Hb levels*			
Male	14.3 ± 0.177	15.14 ± 0.320	0.221
Female	12.7 ± 0.187	12.27 ± 0.453	
Homocysteine levels**			
Normal	21 (70%)	19 (63.33%)	0.154
>Normal	9 (30%)	11 (36.66%)	
Vitamin B12*	418.17 ± 34.03	320.884 ± 28.43	0.034
Folic acid*	10.41 ± 0.59	9.46 ± 0.61	0.296

* Presented as Mean ± SD, ** Presented as n(%)

As shown in Table-1, patients in both studied groups were placed in one of three education groups: low literacy or diploma, bachelor's degree, and master's degree or PhD. As a whole, 31 patients (52.2%) were in the low literacy or diploma group, 16 (26.2%) were bachelor's degree and 13 (21.3%) had a master's degree or PhD. There was no significant relationship in level of education between the two groups. Serum levels of Hb, homocysteine, vitamin B12, and folic acid were measured in both groups (Table-2). The mean serum Hb levels of males and females in both studied groups were 12.48 $\mu\text{m}/\text{dl}$ and 14.72 $\mu\text{m}/\text{dl}$, respectively. As demonstrated in Table-2, the mean serum Hb levels did not differ between patients in the psoriatic and cutaneous-oral lichen planus groups ($P=0.837$). For measuring blood homocysteine level, a cutoff of 15.3 $\mu\text{mol}/\text{l}$ for male patients and 11.6 $\mu\text{mol}/\text{l}$ for female patients was considered. As shown in Table-2, 40 (66.66%) patients in both groups had a normal blood homocysteine level and 20 had a higher than normal blood homocysteine level. The mean blood homocysteine level in psoriatic and cutaneous-oral lichen planus patients was 11.5 $\mu\text{mol}/\text{l}$ and 12.72 $\mu\text{mol}/\text{l}$, respectively. In psoriatic patients, the maximum and minimum blood homocysteine level was 17.02 $\mu\text{mol}/\text{l}$ and 6.14 $\mu\text{mol}/\text{l}$, respectively. Also, in cutaneous-oral lichen planus patients, the maximum and minimum blood homocysteine level was 34.47 $\mu\text{mol}/\text{l}$ and 6.32 $\mu\text{mol}/\text{l}$, respectively. The blood homocysteine level in cutaneous-oral lichen planus patients (12.72 $\mu\text{mol}/\text{l}$) was higher than in psoriatic patients (11.5 $\mu\text{mol}/\text{l}$), but the difference was not statistically significant ($P = 0.364$). However, the blood homocysteine level in psoriatic and cutaneous-oral lichen planus patients was significantly higher than in healthy people ($P = 0.001$). The serum vitamin B12 level in the psoriatic group was significantly higher than in the cutaneous-oral lichen planus patients ($P = 0.034$). As shown in Table-2, both the mean and maximum serum folic acid levels in the psoriatic group were higher than in the cutaneous-oral lichen planus group, but the difference was not significant ($P=0.296$).

Discussion

Elevated plasma homocysteine levels are suggested to be a risk factor for reversible atherosclerotic cardiovascular disease [11]. Hyperhomocysteinaemia is also thought to be an independent risk factor for atherosclerotic cardiovascular diseases, cardiac attack, peripheral vascular obstruction and venous thrombosis [12, 6]. Psoriasis is a chronic inflammatory skin disease with an increased risk of thrombosis and cardiovascular disease. Several studies demonstrated the relationship between increasing cardiovascular risk factors and dermatologic diseases, such as psoriasis, lichen planus, acne rosacea and androgenetic alopecia [13]. In this study, in which we aimed to evaluate and compare serum homocysteine levels in patients with cutaneous-oral lichen planus and psoriasis patients, about 70% of the patients in the psoriasis group had normal plasma homocysteine levels, and in 30%, the levels were higher than normal. However, in the cutaneous-oral lichen planus group, 63.33% of the patients had normal plasma homocysteine levels, and hyperhomocysteinaemia was observed in 36.66% of the patients. However, we found no significant differences in the mean serum homocysteine levels between the two groups. In 2015, Chen *et al.* performed a study to evaluate the association between the deficiencies of Hb, iron, vitamin B12, and folic acid and high blood homocysteine level in patients with OLP [7]. Similarly, their results showed 14.8% of OLP patients had abnormally high blood homocysteine level, which was significantly higher than the healthy control participants [14]. In Saleh *et al.*'s study, serum homocysteine levels were also significantly higher in lichen planus patients than in controls [15]. Additionally, in Sun *et al.*'s study, blood homocysteine levels in patients with atrophic glossitis were higher than in healthy people [16]. Higher blood homocysteine levels in psoriasis patients compared to healthy people have been reported by others [17-19]. In contrast, in Erturan *et al.*'s study (2014), there was no significant difference in serum homocysteine level between psoriasis and chronic plaque

type patients compared to healthy people [20]. Our result was different from that reported in Erturan *et al.*'s study. Nevertheless, our results demonstrated a significant relationship between dermatology diseases and increased serum homocysteine level. With regard to the evidence indicating an association between blood homocysteine level and an increased risk of cardiovascular disease, this finding shows the importance of considering blood homocysteine level in dermatologic disorders. In the present study, although the mean plasma vitamin B12 level was 418.17 in psoriasis patients and 320.884 in cutaneous-oral lichen planus patients, which was in the normal range for both groups, the mean plasma vitamin B12 level in cutaneous-oral lichen planus patients was significantly less than that of the psoriasis patients. In a case-control study, Azizi *et al.* (2013) studied serum levels of vitamin B12 in patients with lichen planus and reported no significant difference in the patient group when compared to the control group [21]. Their finding was similar to the result of our study. However, Sun *et al.* (2012) evaluated the blood vitamin B12 level in 176 atrophic glossitis patients compared with 176 healthy control subjects [16]. They found that atrophic glossitis patients had a significantly higher frequency of vitamin B12 deficiency than healthy control subjects. Also, Brazzelli *et al.* (2010) investigated plasma vitamin B12 levels in 98 patients with chronic plaque psoriasis and 98 healthy controls [17]. They demonstrated that B12 plasma levels were lower in psoriatic patients than in controls; lower levels of vitamin B12 were shown in patients with hyperhomocysteinaemia compared to patients with a normal plasma homocysteine level. We also compared the serum folic acid level in patients with cutaneous-oral lichen planus and psoriasis patients. The mean plasma folic acid level in psoriasis patients was 10.41 ng/ml, and it was 9.46 ng/ml in cutaneous-oral lichen planus patients. Our results showed no significant relationship in mean plasma folic acid level between the two studied groups. However, Chen *et al.* (2015), in a study to assess hematinic deficiencies and pernicious anemia in oral

mucosal disease patients with macrocytosis, revealed that the serum folic acid level in patients with macrocytosis was lower than in normal control participants [14]. In addition, Sun *et al.* (2012) reported that the serum folic acid level was significantly lower in 176 atrophic glossitis patients compared to 176 healthy control subjects [16]. Others have also reported lower serum folic acid levels in chronic psoriasis patients compared to healthy controls [17, 18]. In the present study, among the psoriatic patients, the mean blood Hb levels were 12.7 $\mu\text{m}/\text{dl}$ in women and 14.3 $\mu\text{m}/\text{dl}$ in men, and among cutaneous-oral lichen planus patients, the mean blood Hb levels in women and men were 12.27 $\mu\text{m}/\text{dl}$ and 15.14 $\mu\text{m}/\text{dl}$, respectively. We found no significant difference in blood Hb levels between psoriasis patients and cutaneous-oral lichen planus patients. Chang *et al.* (2015) and Sun *et al.* (2012) reported lower blood Hb levels in patients with oral mucosal disease compared to healthy controls [7, 16]. Higher serum folic acid levels in psoriasis patients compared to healthy controls were also reported by others [18, 17].

Limitations of the Study

The most important limitations of the present study were (i) probable errors in the examination of sample blood, (ii) we don't have a control study because the method of study was analytical and (iii) low sample size, as this limitation may have direct and indirect impact on the generalization of the results. Hence, it is recommended that future studies be carried out with larger samples, using a case control method and more details to gain more accurate results.

Conclusion

According to the results of this study, it can be concluded that in patients with psoriasis or cutaneous-oral lichen planus as chronic inflammatory skin diseases, serum homocysteine levels are higher than in healthy control subjects, but there was no significant difference between the two groups. However, the serum vitamin B12 levels are significantly different. Further studies are

recommended about the course of treatment in patients with psoriasis and lichen planus diseases before therapeutic intervention.

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Conflict of Interests

The authors report that there is no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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