The Effect of Oral Zinc Therapy in Psoriasis Patients with Serum Zinc Deficiency: A Prospective Observational Study

Majid Rostami Mogaddam

Department of Dermatology, Imam Khomeini Hospital, Ardebil University of Medical Sciences, Ardabil, Iran

Nastaran safavi Ardabili

Department of Midwifery, Ardebil Branch, Islamic Azad University, Ardebil, Iran

Nasrollah Maleki (malekinasrollah@gmail.com)

Hematology-Oncology and Stem Cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran https://orcid.org/0000-0003-1511-7052

Research Article

Keywords: Deficiency, Psoriasis, Serum, Thyroid Diseases, Zinc

Posted Date: January 13th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-143898/v1

Abstract

Introduction: Some studies have reported an association between serum zinc levels and psoriasis. This study aimed to assess the serum zinc level and thyroid dysfunction between psoriasis patients and healthy controls. Also, we evaluated the effect of oral zinc therapy in psoriasis patients with serum zinc deficiency.

Materials and Methods: A total of 100 psoriasis patients and 100 healthy age- and sex-matched volunteers were enrolled in this prospective cross-sectional study. Finally, 52 psoriasis patients with serum zinc deficiency were randomly divided into two groups: one in which clobetasol cream alone was treated (group A), and one in which clobetasol cream plus oral zinc sulfate was treated (group B). The treatment response was assessed with Psoriasis Area and Severity Index (PASI) score.

Results: The mean serum zinc level in psoriasis patients and controls was 62.3 ± 14.3 µg/dL and 87.7 ± 35.2 µg/dL, respectively (P-value= .001). Serum zinc deficiency was found in 52% and 26% of psoriasis patients and control subjects, respectively. Thyroid dysfunction was found in 8% of patients with psoriasis compared with 7% in control subjects (P-value=.361). At the end of the 12th week of treatment, the mean value of % reduction from baseline values of PASI Score in group A was 23.8 ± 18.2%, whereas this was 21.31 ± 17.8% in group B (P-value=.486).

Conclusion: Although the prevalence of serum zinc deficiency is higher in psoriasis patients compared with healthy subjects, oral zinc supplementation does not appear to have therapeutic benefits in these patients. Also, we could not find any relationship between thyroid dysfunction and psoriasis.

Introduction

Psoriasis is a chronic inflammatory skin disorder characterized by well-demarcated erythematous plaques covered by silvery-white scales [1]. Prevalence and incidence of psoriasis vary in different parts of the world. A systematic review of published population-based studies found that the occurrence of psoriasis varied according to age, geographic region, and demographic characteristics. The prevalence of psoriasis in adults ranged from 0.91% to 8.5%, and in children from 0% to 2.1%. The incidence of psoriasis in adults ranged from 78.9 to 230 cases per 100,000, and in children, the reported incidence estimate was 40.8 cases per 100,000 [2]. In another recently published systematic review, the estimates of the prevalence of psoriasis in adults ranged from 0.51% to 11.43%, and in children from 0% to 1.37% [3]. About 7.4 million American adults were affected by psoriasis in 2013, and the prevalence of psoriasis among adults in the United States has been estimated to be 3.2 percent [4]. There are no clear race, ethnicity, or gender predilections for psoriasis. Although psoriasis affects people of all ages, it seems to be two peaks in the age of onset: a first peak in the age group 30 to 39 years and a second peak in the age group 50 to 60 years [2]. In recent years, great advances have been made in the understanding of psoriasis pathogenesis. It is known that the combination of environmental triggers, genetic

predisposition, and innate immune response initiate the pathogenesis of psoriasis that results in an adaptive immune response [5].

Zinc is an essential trace element that is necessary for growth at all stages of life and plays a key role in the functioning of the immune system, physical growth and development, reproductive health, sensory function, and neurobehavioral development [6]. Zinc deficiency is a serious health problem worldwide affecting developed as well as developing countries [7]. The estimated global prevalence of zinc deficiency is 17.3% [8] and ranges from 11% to 80% [9]. Prevalence of serum zinc deficiency and dietary zinc inadequacy seems to be lower in Iranians, compared to some other populations. In Iran, the estimated prevalence of zinc deficiency is 3.0 and 2.4 % in men and women, respectively [10].

Some investigators have reported an association between low serum zinc levels and a variety of dermatological conditions including acne vulgaris, rosacea, psoriasis, vitiligo, leprosy, warts, cutaneous leishmaniasis, alopecia areata, hidradenitis suppurativa, oral aphthosis, and Behcet's disease [11, 12]. It has been shown that in the majority of skin disorders associated with zinc deficiency, oral zinc supplementation seems to be a safe and effective treatment in improving symptoms [11]. There are not many studies of serum zinc levels in patients with psoriasis. Some researchers have reported the effectiveness of oral zinc therapy in psoriasis patients, while others have not found the same [13, 14]. Also, it has been reported that a topical formulation of zinc pyrithione can be used for the treatment of localized psoriasis [15]. This study was conducted to assess the serum level of zinc in patients with psoriasis and to evaluate the thyroid dysfunction in psoriasis. Also, we evaluated the effect of oral zinc therapy in psoriasis patients with serum zinc deficiency.

Methods And Materials

Design and population

The study was approved by the Ethics Committee of the Ardabil University of Medical Sciences. This was a prospective cross-sectional study. Patients presenting with psoriasis to the dermatology outpatient clinic of Imam Khomeini Hospital in Ardabil, Iran between May 2013 and January 2018 were recruited for the study subjects. A total of 100 patients with psoriasis and 100 healthy controls were included. The two groups were matched for age and sex. The diagnosis of psoriasis was made clinically based on the history and characteristic appearance of erythematous papules and plaques with a silver scale in common locations such as the scalp, elbows, knees, and back.

A total of 200 participants 15 or more years old were enrolled in this study. All patients were assessed by a thorough history, physical examination, and routine laboratory investigations. Patients were examined to assess the clinical type of the disease and its surface area. Patients who met each of the following criteria were excluded from the study [16]: (1) under any treatment with zinc in the one month prior to diagnosis; (2) gastrointestinal disease associated with chronic diarrhea ; (3) Liver dysfunction; (4) renal failure; (5) heart failure; (6) history of alcohol abuse; (7) history of active malignancy; (8) malabsorption disorders; (9) pregnancy; (10) under immunosuppressive treatment; (11) history of vegetarian diet within

1 month prior to the study; (12) subjects suffering from other pigmentation disorders; (13) under any treatment with a topical or inhaled corticosteroid or systemic steroids within 1 month prior to the study; (14) diabetes mellitus; (15) receiving any medication that could change serum levels of zinc such as chelating agents, glucocorticoids, diuretics, clofibrates, or supplements; and (16) under any treatment with topical hydroquinone, isotretinoin or with any drugs that can induce hyperpigmentation within 1 months prior to the study. Written informed consent was obtained from the participants.

Data collection

A questionnaire was completed for each patient, which included the data of demographic status, medical and drug history, extension and duration of psoriasis, and familial status for psoriasis. Then, for all participants, laboratory tests were recommended, which comprised complete blood count, fasting blood sugar, serum levels of zinc, calcium, albumin, 25-hydroxy vitamin D3, phosphorus, liver function, renal function, and thyroid function tests.

Measurement of serum zinc level

All subjects (psoriasis patients and healthy controls) were investigated for the measurement of serum zinc level. A 5 ml intravenous blood sample was taken from eligible cases and controls. Supernatant serums were separated by centrifugation for 10 min at 4000 rpm and stored at − 40°C until time of analysis. Blood samples were withdrawn by zinc-free plastic syringes and placed in zinc-free centrifuge tubes. A serum zinc concentration was assayed by atomic absorption spectrophotometry (Spectra AA 10 plus, Varian, Dickinson, Texas, USA) using commercial kits (Zinc Assay Kit, Elitech, France). The normal value of serum zinc level in adults was accepted as 68 - 107 micrograms per deciliter. Zinc deficiency was defined as a serum zinc level of fewer than 68 micrograms per decilitre.

Assessment of response to treatment

A number of scoring systems have been proposed to evaluate the severity of psoriasis. Psoriasis Area and Severity Index (PASI) score is one of the most widely used instruments for measuring the severity of psoriasis [16]. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease), with higher scores indicating more severe disease. The body was divided into four sections head (10% of a person's skin); arms (20% of a person's skin); trunk (30% of a person's skin); legs (40% of a person's skin). Each of these areas was scored by itself, and then the four scores were combined into the final PASI. For each section, the percent of the area of skin involved was estimated and then transformed into a grade from 0 to 6: (0) 0% of the involved area, (1) less than 10% of the involved area, (2) 10–29% of the involved area, (3) 30–49% of the involved area, (4) 50–69% of the involved area, (5) 70–89% of the involved area, and (6) more than 90% of the involved area. In addition, within each area, the severity was estimated by three clinical signs (erythema, induration, and scaling). Severity was evaluated on a scale of 0 (none), 1 (mild), 2 (moderate), 3 (severe), 4 (very severe).

Intervention

In this double-blinded randomized control study, psoriasis patients with serum zinc deficiency were randomly divided into two groups: The patients in group A were treated with 0.05% clobetasol propionate cream twice daily alone, and patients in group B were treated with 0.05% clobetasol propionate cream twice daily plus oral zinc sulfate (220 mg twice daily). The treatment for the two groups continued after 12 weeks. PASI score was measured before and after the treatment period. Evaluation of the response after 12 weeks of treatments was presented as a % reduction from baseline values of PASI Score.

Statistical Analysis

The statistical analysis of the data was done using the SPSS software for Windows, version 21 (SPSS Inc., Chicago, IL, United States). A P-value of < 0.05 was considered statistically significant. Quantitative variables were expressed as means ± standard deviations. The comparison of the continuous variables was accomplished with Student's t-test, and, for the comparison of the categorical variables, the Pearson chi-squared test ($\chi 2$ test) and Fisher exact test were used. The results were expressed as means ± standard deviations.

Results

Baseline characteristics

A total of 100 patients with psoriasis and 100 healthy volunteers were enrolled in this study. Of the 100 patients with psoriasis, 58 (58%) were men, and 42 (42%) were women, whereas of the 100 healthy subjects, 59 (59%) were men, and 41 (41%) were women. In the psoriasis group, 64 patients (64%) were single and 36 patients (36%) were married, while in the control group, 59 patients (59%) were single and 41 patients (41%) were married, and there was no significant difference between the groups in terms of marital status. The mean age of the psoriasis patients was 29.49 ± 5.46 years with an age range of 17 to 68 years, whereas the mean age of the controls was 30.42 ± 6.51 years with an age range of 16 to 71 years. The two groups showed no significant differences in age or gender. Among the patients with psoriasis, chronic plaque-type was seen in 98% of cases, and postular type in 2% of cases. A positive family history of psoriasis in first degree relatives was present in 79 (79%) of the cases. The mean duration of the disease was 13.25 ± 7.06 days, with a range between 2 and 30 days.

Prevalence of psoriasis by age group

In the control group, 75 subjects (75%) were less than 45 years and 25 subjects (25%) above 45 years old, while in the psoriatic group, 74 patients (74%) were less than 45 years and 26 patients (26%) above 45 years old. The maximum age ranges in both groups were between the ages of 25–35 years so that the control group included 30 subjects (30%) aged 25-35 years, whereas the psoriatic group included 31 patients (31%) aged 25-35 years. The age distribution of psoriasis patients and the control group are shown in **Table 1**.

Prevalence of serum zinc level

Serum zinc levels in psoriasis patients and control subjects were presented in **Table 2**. Serum zinc levels in control subjects ranged from 64 to 128 micrograms per deciliter with a mean value of 87.7 ± 35.2 micrograms per deciliter, whereas serum zinc levels in psoriasis patients ranged from 41 to 95 micrograms per deciliter with a mean value of 62.3 ± 14.3 micrograms per deciliter. Paired t-test results showed that there is a significant difference between zinc serum levels in psoriasis patients compared with healthy subjects (p-value = 0.001). Serum zinc deficiency was found in 52% and 26% of psoriasis patients and control subjects, respectively.

Correlation between serum zinc levels and extent of the skin lesions

In addition, the mean extent of the skin lesions was 424.53 ± 289.29 cm2, with a range between 27.5 and 960 cm2. The data analysis showed that there is no significant relationship between serum zinc level and duration of disease in patients with psoriasis (p-value=0.63). However, a significant relationship was observed between serum zinc level and extent of skin lesion (p-value=0.001), so that decreased serum zinc level is concomitant with the increased extent of skin lesion.

Evaluation of thyroid dysfunction in psoriasis patients

Among patients with psoriasis, 8 (8%) had thyroid dysfunction, while in the control subjects, 7 (7%) had thyroid dysfunction. There was no significant correlation between serum zinc level with thyroid dysfunction in patients with psoriasis compared with the control group (P = 0.361). The prevalence of thyroid dysfunction in psoriasis patients compared with the control group is shown in **Table 3**. None of the mean serum levels of calcium, phosphorus, FBS, liver, and renal function tests showed any statistically significant differences in patients with psoriasis compared with the control group.

The effect of treatment

In the present study, 52 patients with psoriasis had a serum zinc deficiency. At week 12 of treatment, all patients completed the trial. All the patients were randomly allocated into two groups, one in which 0.05% clobetasol propionate cream (group A, n= 26) was treated and one in which 0.05% clobetasol propionate cream plus oral zinc sulfate (group B, n= 26) was treated. The two groups were matched for age and gender (34 male, 18 female; mean age: 28.14 ± 6.27 years). As the groups were originally matched for age and gender, differences in their mean age and gender were not statistically significant.

The mean values of PASI score before and after treatment in both groups of patients are shown in **Table 4.** At week 12 of treatment, the mean value of % reduction from baseline values of PASI Scores in patients on 0.05% clobetasol propionate cream (group A) was 23.8 ± 18.2%, whereas this was 21.31 ± 17.8% in patients on 0.05% clobetasol propionate cream plus oral zinc sulfate (group B). However, our results showed that there was no significant difference in % reduction from baseline values of PASI score between the two groups.

Discussion

There are several types of psoriasis that plaque-type psoriasis, occurring in 85%–90% of affected patients, is the most common form of psoriasis. Guttate psoriasis occurs in about 10% of patients, and erythrodermic and pustular types each occur in fewer than 3% of patients [17]. In our study, chronic plaque-type psoriasis was seen in 98% of cases, and postular type in 2% of cases. Previous studies reported that the prevalence of a positive family history of psoriasis in first-degree relatives ranged from 4.5 to 91% [18]. In the current study, a positive family history of psoriasis in first degree relatives was present in 79% of the cases.

There was a lack of agreement in the published studies about whether the prevalence of psoriasis differed between men and women. The results of a recent meta-analysis showed that there are no differences in the frequency of psoriasis between genders were found in the United States, United Kingdom, Norway, Spain, Scotland, and Taiwan in individuals of all ages combined. On the other hand, other studies reported a slightly higher prevalence of psoriasis in female subjects than male subjects in Swedish and Germany. In contrast, psoriasis was more frequent in men than in women in Denmark, Australia, Sweden, and China [2]. In the present study, approximately three-fourths of patients with psoriasis had less than 45 years of age, and the majority of patients were seen in the age range of 25 to 35 years. The findings were in line with those reported in other studies. Recent reports indicate that the two-peak age of onset is considered for psoriasis; the early age of onset is between 20 to 29 or 30 to 39 years of age, and the second with a peak value around 60 years, after which the prevalence reduced. Psoriasis is uncommon before the age of 9 years [2].

The results observed in the present study showed a significant reduction in serum zinc level in psoriasis patients as compared to healthy subjects. We hypothesize that this could have happened for two reasons: first, it is possible that the decrease in serum zinc level in psoriasis patients may exacerbate the disease. Secondly, the progression of psoriasis may be associated with a reduction in serum zinc level. In agreement with the findings of our investigation, some researchers have reported significantly low serum zinc levels in psoriatic patients [19-21], although other authors found no such difference [22, 23]. For example, a study in Germany found that in contrast to the data given in the literature, there was no significant difference between serum zinc level in patients with atopic dermatitis and psoriasis Vulgaris compared with healthy subjects. They suggested that zinc replacement therapy in patients with atopic dermatitis and psoriasis appears to be indicated only in those with a documented zinc deficiency [24]. In our study, a reverse relationship was observed between serum zinc level and the extent of a skin lesion in patients with psoriasis. Indeed, a greater extent of skin involvement was correlated with lower serum zinc levels. This is in agreement with the results of Nigam [25], who showed that patients with more than 20% body surface area involvement were significantly decreased serum zinc concentration compared with those with less than 20% body surface area involvement.

In order to determine the relationship between plasma zinc level and the extent of skin involvement in psoriasis, McMillan, and Rowe [26] evaluated plasma zinc, serum albumin, and alkaline phosphatase (a

zinc-dependent enzyme) were measured in 35 psoriatic patients as compared with age- and sex-matched healthy controls. There was no significant difference between these two groups as a whole for plasma zinc level, but psoriatic patients with less than 10% body surface area involvement had significantly higher mean plasma zinc levels compared with the control group. In addition, a significant relationship was observed between the extent of surface involvement and the plasma zinc level, those with more than 10% body surface area involvement having lower levels than those with less than 10% body surface area involvement. These findings are consistent with the results of our study [26]. Some researchers have demonstrated that the zinc content of neutrophils is significantly reduced in patients with psoriasis compared with both healthy subjects and patients with seborrhoeic dermatitis, which this reduction was unrelated to the extent of skin involvement [27]. However, zinc levels of plasma and erythrocyte were unchanged.

Zinc supplementation can have a valuable role in patients with psoriasis. It has been suggested that oral zinc sulfate at a total dose of 120 mg/day of elemental zinc, for 6 months may be an effective and well-tolerated disease-modifying anti-rheumatic drug (DMARD) in psoriatic arthritis [28]. In a previous study, the researchers found that oral zinc sulfate seems to be valuable in the treatment of psoriatic arthritis [13]. In addition, another study evaluated the efficacy of a topical formulation of 0.25% zinc pyrithione in an emollient base compared with an emollient alone in the treatment of patients with localized psoriasis involving less than 10% of body skin areas. However, the results observed in this study showed a topical formulation of zinc pyrithione can be used to treat localized psoriasis [15]. These findings are not consistent with the results of the present study. Our study showed that oral zinc sulfate (220 mg twice daily) is not effective in psoriasis patients with serum zinc deficiency. In line with this result, Voorhees et al. [29], reported oral zinc therapy in psoriasis no better than placebo though it did increase zinc concentration in psoriatic scales, uninvolved skin, and urine. In addition, Housman et al. [30] found topical 0.25% zinc pyrithione spray does not appear to enhance the efficacy of clobetasol propionate 0.05% foam after 2 weeks of therapy. These findings support our study results.

Some investigators have reported an association between thyroid dysfunction and a variety of dermatological conditions [31]. There is currently no evidence to support an association between thyroid dysfunction and psoriasis. The present study demonstrated thyroid dysfunction in 8% of patients with psoriasis compared with 7% in control subjects, however; the difference was not statistically significant. In line with this result, Gul et al. [32], reported thyroid autoimmunity in patients with psoriasis who did not have arthritis was no different from that found in healthy individuals. Most researchers have reported that there is no connection between thyroid dysfunction and psoriasis. For example, a study by Vassilatou et al. [33] evaluated prospectively 114 psoriatic patients, 30 of them with psoriatic arthritis, and 286 subjects without psoriasis or known thyroid disease or autoimmune disease. Autoimmune thyroiditis in psoriatic patients was not related to the age of psoriasis onset, psoriasis duration, PASI score, psoriatic arthritis, and obesity. They eventually concluded that psoriatic patients with or without psoriatic arthritis do not have an increased risk for autoimmune thyroiditis. These findings are consistent with the results of our study.

Another study [34] evaluated prospectively 100 psoriatic patients compared with a control group of 54 patients, without known thyroid gland abnormalities. These authors found no significant difference in the thyroid gland functions between the psoriatic and the control patients. They observed that in patients with severe psoriasis, there are increased TSH levels and positive auto-antibodies titer compared to patients with mild psoriasis. In contrast, some researchers have reported thyroid function follow-up and suitable treatments should be performed regularly in female patients at high risk, especially those who have thyroid-stimulating hormone within the normal range but at the higher limit, those with positive anti-thyroid peroxidase antibodies, and those who have a small hypoechoic thyroid pattern in ultrasound [35].

The present study has several limitations that should be considered. First, this study was a single-center with a limited sample size and these results may not be generalizable to other centers. Large-scale population studies are necessary in order to confirm these observations. Second, Serum zinc level measurement may be affected by several factors, including stress, infection, or other metabolic conditions [36].

Conclusion

Although the prevalence of serum zinc deficiency is higher in psoriasis patients compared with healthy subjects, oral zinc supplementation does not appear to have therapeutic benefits in these patients. In addition, we could not find any relationship between thyroid dysfunction and psoriasis.

Declarations

Author contributions: M.R. Mogaddam contributed to the conception and design of the research; N. Maleki contributed to the design of the research; N.S. Ardabili contributed to the acquisition and analysis of the data; M.R. Mogaddam and N. Maleki contributed to the interpretation of the data, and drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Financial Disclosure: We declare that there is No Financial Disclosure in our article.

Conflict of Interest: We declare that there is No Conflict of Interest in our article.

Funding: This study was approved by the Ethics Committee of the Ardebil University of Medical Sciences, Ardebil, Iran. Institutional approval Code: IR.ARUMS.REC.1390.2922

Informed consent: Informed consent was obtained from all individual participants included in the study.

Conflict of Interest: We declare that there is no conflict of interest in our article. This study was approved by the Ethics Committee of the Ardebil University of Medical Sciences, Ardebil, Iran.

Ethical approval: Ethics approval was obtained for this study from the Ethics Committee of the Ardebil University of Medical Sciences. Informed consent was obtained from all individual participants included

in the study.

References

1. Krueger JG, Bowcock A. Psoriasis pathophysiology: current concepts of pathogenesis. Ann Rheum Dis. 2005;64 Suppl 2:ii30-6.
2. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated Comorbidity (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013 ;133(2):377-85.
3. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017;31(2):205-212.
4. Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol. 2014;70(3):512-6.
5. Schäkel K, Schön MP, Ghoreschi K. Pathogenesis of psoriasis. Hautarzt. 2016;67(6):422-31.
6. Roohani N, Hurrell R, Kelishadi R, Schulin R. Zinc and its importance for human health: An integrative review. J Res Med Sci. 2013;18(2):144-57.
7. Salgueiro MJ, Weill R, Zubillaga M, Lysionek A, Caro R, Goldman C, et al. Zinc deficiency and growth: current concepts in relationship to two important points: intellectual and sexual development. Biol Trace Elem Res. 2004;99(1-3):49-69.
8. Wessells KR, Brown KH. Estimating the global prevalence of zinc deficiency: results based on zinc availability in national food supplies and the prevalence of stunting. PLoS One. 2012;7(11):e50568.
9. Galetti V, Mitchikpè CE, Kujinga P, Tossou F, Hounhouigan DJ, Zimmermann MB, et al. Rural Beninese Children Are at Risk of Zinc Deficiency According to Stunting Prevalence and Plasma Zinc Concentration but Not Dietary Zinc Intakes. J Nutr. 2016;146(1):114-23.
10. Ghasemi A, Zahediasl S, Hosseini-Esfahani F, Azizi F. Reference values for serum zinc concentration and prevalence of zinc deficiency in adult Iranian subjects. Biol Trace Elem Res. 2012;149(3):307-14.
11. Mogaddam MR, Ardabili NS, Maleki N, Chinifroush MM, Fard EM. Evaluation of the serum zinc level in patients with vitiligo. Postepy Dermatol Alergol. 2017;34(2):116-119.
12. Rostami Mogaddam M, Safavi Ardabili N, Maleki N, Soflaee M. Correlation between the severity and type of acne lesions with serum zinc levels in patients with acne vulgaris. Biomed Res Int. 2014;2014:474108.
13. Clemmensen OJ, Siggaard-Andersen J, Worm AM, Stahl D, Frost F, Bloch I. Psoriatic arthritis treated with oral zinc sulphate. Br J Dermatol. 1980;103(4):411-5.
14. Burrows NP, Turnbull AJ, Punchard NA, Thompson RP, Jones RR. A trial of oral zinc supplementation in psoriasis. Cutis. 1994;54(2):117-8.
15. Sadeghian G, Ziaei H, Nilforoushzadeh MA. Treatment of localized psoriasis with a topical formulation of zinc pyrithione. Acta Dermatovenerol Alp Pannonica Adriat. 2011;20(4):187-90.

16. Fredriksson T, Pettersson U. Severe psoriasis--oral therapy with a new retinoid. Dermatologica. 1978;157(4):238-44.
17. Lebwohl M. Psoriasis. Lancet. 2003;361(9364):1197-204.
18. Fotiadou C, Lazaridou E, Ioannides D. Management of psoriasis in adolescence. Adolesc Health Med Ther. 2014;5:25-34.
19. Greaves M, Boyde TR. Plasma-zinc concentrations in patients with psoriasis, other dermatoses, and venous leg ulceration. Lancet. 1967;2(7524):1019-20.
20. Arora PN, Dhillon KS, Rajan SR, Sayal SK, Das AL. Serum Zinc Levels in Cutaneous Disorders. Med J Armed Forces India. 2002;58(4):304-6.
21. Morgan ME, Hughes MA, McMillan EM, King I, Mackie RM. Plasma zinc in psoriatic in-patients treated with local zinc applications. Br J Dermatol. 1980;102(5):579-83.
22. Hinks LJ, Young S, Clayton B. Trace element status in eczema and psoriasis. Clin Exp Dermatol. 1987;12(2):93-7.
23. Molokhia MM, Portnoy B. Neutron activation analysis of trace elements in skin. V. Copper and zinc in psoriasis. Br J Dermatol. 1970;83(3):376-81.
24. Kreft B, Wohlrab J, Fischer M, Uhlig H, Skölziger R, Marsch WC. Analysis of serum zinc level in patients with atopic dermatitis, psoriasis vulgaris and in probands with healthy skin. Hautarzt. 2000;51(12):931-4.
25. Nigam PK. Serum zinc and copper levels and Cu: Zn ratio in psoriasis. Indian J Dermatol Venereol Leprol. 2005;71(3):205-6.
26. McMillan EM, Rowe D. Plasma zinc in psoriasis: relation to surface area involvement. Br J Dermatol. 1983;108(3):301-5.
27. Leung RS, Turnbull AJ, Taylor JA, Russell-Jones R, Thompson RP. Neutrophil zinc levels in psoriasis and seborrhoeic dermatitis. Br J Dermatol. 1990;123(3):319-23.
28. Frigo A, Tambalo C, Bambara LM, Biasi D, Marrella M, Milanino R, Moretti U, Velo G, De Sandre G. Zinc sulfate in the treatment of psoriatic arthritis. Recenti Prog Med. 1989;80(11):577-81.
29. Voorhees JJ, Chakraborty SG, Fernando BML. Zinc therapy and distribution in psoriasis. Arch Der. 1969;100:669–673.
30. Housman TS, Keil KA, Mellen BG, McCarty MA, Fleischer AB Jr, Feldman SR. The use of 0.25% zinc pyrithione spray does not enhance the efficacy of clobetasol propionate 0.05% foam in the treatment of psoriasis. J Am Acad Dermatol. 2003;49(1):79-82.
31. Rostami Mogaddam M, Iranparvar Alamdari M, Maleki N, Safavi Ardabili N, Abedkouhi S. Evaluation of autoimmune thyroid disease in melasma. J Cosmet Dermatol. 2015;14(2):167-71.
32. Gul U, Gonul M, Kaya I, Aslan E. Autoimmune thyroid disorders in patients with psoriasis. Eur J Dermatol. 2009;19(3):221-3.
33. Vassilatou E, Papadavid E, Papastamatakis P, Alexakos D, Koumaki D, Katsimbri P, et al. No association of psoriasis with autoimmune thyroiditis. J Eur Acad Dermatol Venereol. 2017;31(1):102-

106.
34. Zoabi A, Ziv M, Rozenman D, Lovoshitski R. Prevalence of thyroid abnormalities among psoriatic patients. Harefuah. 2012;151(10):566-9, 605-6.
35. Fallahi P, Ferrari SM, Ruffilli I, Elia G, Miccoli M, Sedie AD, et al. Increased incidence of autoimmune thyroid disorders in patients with psoriatic arthritis: a longitudinal follow-up study. Immunol Res. 2017;65(3):681-686.
36. King JC. Assessment of zinc status. J Nutr. 1990;120 Suppl 11:1474-9.

Tables

Table 1: Age distribution of patients

	Age groups (years)					
Groups	15 to 25	25 to 35	35 to 45	45 to 55	55 to 65	65 to 75
Control, n (%)	26 (26%)	30 (30%)	19 (19%)	15 (15%)	7 (7%)	3 (3%)
Case, n (%)	25 (25%)	31 (31%)	18 (18%)	15 (15%)	7 (7%)	4 (4%)
Total, n (%)	51 (25.5%)	61 (30.5%)	37 (18.5%)	30 (15%)	14 (7%)	7 (3.5%)

Table 2: The serum zinc level in psoriasis patients and controls.

Study subjects	Serum zinc level (µg/dL)		p value
	Range	Mean ± SD	
Psoriasis group (n = 100)	41 to 95	62.3 ± 14.3	0.001
Control group (n= 100)	64 to 128	87.7 ± 35.2	

Table 3: Prevalence of thyroid dysfunction in psoriasis patients compared with control group

Groups	Number of normal thyroid function (%)	Number of hypothyroidism (%)	Number of hyperthyroidism (%)	p value
Psoriatic group (n = 100)	92 (92%)	7 (7%)	1 (1%)	0.361
Control group (n = 100)	93 (93%)	5 (5%)	2 (2%)	

Table 4: Mean values of PASI score before, after treatment, and mean differences in both groups of patients.

Groups	PASI score (Mean ± SD)		Differences (Mean ± SD)	P-value
	Before treatment	12 weeks after treatment		
Clobetasol propionate cream (group A)	5.6 ± 1.9	1.4 ± 0.7	4.6 ± 3.1	p<0.001
Clobetasol propionate cream plus oral zinc sulphate (group B)	6.1 ± 2.3	1.3 ± 0.4	4.9 ± 3.4	p<0.001
p-value between groups before and after treatment	p =0.314	p =0.416	p =0.486	