Serum Zinc Level in Vitiligo: A Case-control Study

Mina Mirnezami, Hoda Rahimi

Abstract

Background: Vitiligo is characterized by the idiopathic destruction of melanocytes, probably of autoimmune etiology, that results in depigmented patches of skin and mucosal surfaces. Oxidative stress may contribute to the pathogenesis of vitiligo. Zinc, a trace element with antiapoptotic properties, plays a major role in the process of melanogenesis and elimination of free radicals. The present study was conducted with the aim of comparing serum zinc levels in patients with vitiligo and in normal controls. Materials and Methods: In this case-control study, we studied 103 patients with vitiligo and 103 healthy sex-and age-matched controls. Serum zinc levels were measured in these two groups using atomic absorption spectrophotometry and compared with each other. Results: The mean serum zinc level was 92.1 mcg/dl in the focal vitiligo, 81.3 mcg/dl in the generalized vitiligo, and 91.8 mcg/dl in the control group. A significant difference in serum zinc levels was observed between the patients with generalized vitiligo and the controls. Lower serum zinc levels were also correlated with longer duration of the disease. Furthermore, a negative relationship was found between serum zinc level and age of patients with vitiligo. Conclusion: Serum zinc level is low in patients with generalized vitiligo. In these patients, serum zinc level is in negative correlation with patient’s age and disease duration.

Keywords: Melanocyte, pigment, vitiligo, zinc

Introduction

Vitiligo is one of the most prevalent pigmentation disorders in the world characterized by the destruction of melanocytes and the development of white macules and patches on the skin or mucosa. With a global frequency of 0.5%–4%, vitiligo occurs in both sexes and all races and ages. Nevertheless, the most common age of onset of the disease is 10–30 years. Since patches of depigmentation mainly develop in the exposed areas of the body, mostly in young individuals, vitiligo can be associated with lower self-confidence, disturbed social and sexual performance, isolation, depression, and ultimately lower quality of life.

Although the mechanisms involved in the pathogenesis of vitiligo are not fully understood, it is hypothesized that oxidative stress can play a major role in its pathogenesis. In fact, some mediators such as hydrogen peroxide, which are produced in the biosynthesis of melanin, are toxic for melanocytes. If not eliminated by the antioxidant system, these mediators can destroy melanocytes.

Zinc is a rare element with many vital functions in human body. While the apoptosis of melanocytes has been suggested as a possible cause of vitiligo, zinc is known to have antiapoptotic property. Moreover, zinc and other trace elements are known as antioxidants that neutralize the toxic effects of free radicals. Zinc is also involved in the process of melanogenesis.

Due to the unclear etiology of vitiligo, the proposed treatments have been unsuccessful and unsatisfactory. Considering the significant burden of vitiligo, a combination of routine treatments and alternative therapies would be required to promote the patients’ quality of life.

What was known?

• Oxidative stress may play a role in pathogenesis of vitiligo.
• Apoptosis of melanocytes is a possible cause of vitiligo.
• Zinc has both antiapoptotic and antioxidative effects.

From the Department of Dermatology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran ‘Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Address for correspondence:
Dr. Hoda Rahimi, Skin Research Center, Shohada-e Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Shahrdari St, 1989934148 Tehran, Iran.
E-mail: hoda_rahimi@yahoo.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Mirnezami M, Rahimi H. Serum zinc level in vitiligo: A case–control study. Indian J Dermatol 2018;63:227-30.

Received: July, 2016. Accepted: January, 2018.
quality of life. However, previous studies have reported contradictory results about serum zinc levels in patients with vitiligo. Therefore, the present study was conducted with the specific objective of evaluation of serum zinc level in patients with vitiligo and comparison with that of controls.

Materials and Methods

In this case–control study, 103 patients with vitiligo who presented to our dermatology clinic from April 2015 to April 2016 were selected for the study. The control group included 103 age- and sex-matched healthy individuals who were selected from either patients’ family members or from medical staffs. The study protocol was approved by our medical ethics committee. The participants were asked to sign an informed consent form after they were provided with complete information about the study protocol. Patients with vitiligo who had not received zinc supplements over the past 4 weeks and did not have any other dermatologic or systemic diseases were included in the study. Patients with cirrhosis, malignancies, renal failure, diarrhea, acute infections, alcohol users, women-receiving contraceptive pills, and pregnant women were excluded from the study.

Demographic information and history of underlying diseases were recorded. Vitiligo was divided into three subtypes: generalized vitiligo (widespread lesions with almost symmetrical distribution), focal vitiligo (one or few lesions at a single site), and mucosal vitiligo (involvement of mucosa membranes). Serum zinc levels were measured in these groups and in controls using atomic absorption spectrophotometry.

The analysis of variance (ANOVA) test was performed to compare the serum zinc levels in the case and control groups. We also used independent t-test to compare serum zinc levels in focal and generalized vitiligo. P<0.05 was considered statistically significant.

Results

Of 103 patients with vitiligo, 31.1% were male and 68.9% were female. Generalized, focal, and mucosal vitiligo were seen in 63 (61.2%), 39 (37.9%), and 1 (1%) of the patients, respectively. Moreover, 29.1% of the patients had a family history of generalized vitiligo. A family history of thyroid disorders (either hypothyroidism or hyperthyroidism) and type II diabetes was reported by 19.4% and 27.2% of the patients, respectively.

The mean serum zinc levels were 92.1, 81.3, and 91.8 mcg/dl in the focal vitiligo, generalized vitiligo, and the control groups, respectively. Independent sample's t-test was applied to compare the means of serum zinc levels in these groups. While patients with focal vitiligo were similar to the control group in terms of serum zinc level, individuals with generalized vitiligo had significantly lower zinc level in comparison with the control group (P=0.031) [Tables 1-3].

A negative correlation was observed between serum zinc level and age in patients with vitiligo (R=-0.67). Furthermore, there was a strong positive correlation between disease duration and serum zinc levels in both generalized and focal vitiligo (R=0.73). In other words, patients with longer duration of the disease had lower zinc level.

Moreover, significant lower zinc level was observed in patients with generalized vitiligo in comparison with focal vitiligo (P=0.003).

Discussion

Vitiligo is a common pigmentary disease of the skin and mucous membrane and is characterized by depigmented macules and patches. It usually begins in young adulthood.[1,2] Since patches of depigmentation mainly develop in the exposed areas of the body, mostly in young individuals, vitiligo can be associated with lower self-confidence, disturbed social and sexual performance, isolation, depression, and ultimately lower quality of life.[1,2,5]

Similar male-to-female ratios have been reported in the most previous studies in patients with vitiligo. For instance, in a study by Yaghoobi et al., female and male patients comprised 45.3% and 54.7% of the study population, respectively.[6] However, Shameer et al. evaluated 60 patients and found vitiligo to be more frequent in men (male-to-female ratio equal to 4.5:1). In

Table 1: Serum zinc levels in patients with different types of vitiligo

| Type of Vitiligo | n  | Mean serum zinc level (mcg/dl) | SD | P    |
|-----------------|----|-------------------------------|----|------|
| Focal vitiligo  | 39 | 92.1                          | 13.8| 0.023|
| Generalized vitiligo | 63 | 81.3                          | 12.7|      |

SD: Standard deviation

Table 2: Serum zinc levels in patients with focal vitiligo and the control group

| Type of Vitiligo | n  | Mean serum zinc level (mcg/dl) | SD | P    |
|-----------------|----|-------------------------------|----|------|
| Focal vitiligo  | 39 | 92.1                          | 13.8| 0.681|
| Control         | 103| 91.8                          | 16.2|      |

SD: Standard deviation

Table 3: Serum zinc levels in patients with generalized vitiligo and the control group

| Type of Vitiligo | n  | Mean serum zinc level (mcg/dl) | SD | P    |
|-----------------|----|-------------------------------|----|------|
| Generalized vitiligo | 63 | 81.3                          | 12.7| 0.031|
| Control         | 103| 91.8                          | 16.2|      |
the present research, vitiligo was more common in women (female: 68.9%; male: 31.1%). This finding can be due to the fact that women tend to care more about their skin problems and are more likely to visit dermatology clinics. Hypothesized mechanisms involved in vitiligo are autoimmune factors, intrinsic defects of melanocytes, oxidative stress, cytotoxic mechanisms, and neural mechanisms. Several studies revealed that oxidative stress may play a major role in the pathogenesis of vitiligo. They suggest that the accumulation of free radicals is toxic to melanocytes and results in their destruction. Zinc is known as a potential antiapoptotic agent. Apoptosis of melanocytes may be involved in the pathogenesis of vitiligo. Thus, zinc may be a promising agent in the treatment of vitiligo by preventing apoptosis of melanocytes. Zinc and other micronutrients have a key role in the process of melanogenesis. They catalyze the production of 5, 6-dihydroxy indole-2-carboxylic acid and enhance the formation of eumelanin polymer from monomers. This process is the final stage of eumelanin formation in melanogenesis, so zinc may have an important effect on vitiligo.

Family history of vitiligo was positive in 29.1% of our patients. Likewise, Shameer et al. reported a positive family history in 33% of patients with vitiligo. Patients with focal and mucosal vitiligo comprised 37.9% and 1% of the cases, respectively. Similar to Shameer et al., we found generalized vitiligo to be the most frequent type of vitiligo. The mean of serum zinc levels were 92.1, 81.3, and 91.8 mcg/dl in focal vitiligo, generalized vitiligo, and the control groups, respectively. While patients with focal vitiligo and the control group had no significant difference in terms of serum zinc levels, participants with generalized vitiligo had significantly lower zinc levels compared to the control group. These findings are in agreement with those previously reported by Shameer et al. Arora et al. failed to detect any significant difference between serum zinc levels in the case and the control groups while Helmy et al. found higher serum levels in the case group. Yaghoobi et al. reported serum zinc levels to be normal, in most of their vitiligo patients. However, due to the absence of a control group in this study, their findings are not comparable to ours. Shameer et al. found that low zinc levels were more frequent in patients with disease duration of 2–5 years. In this study, duration of the disease had a strong positive linear relationship with serum zinc levels. In fact, longer durations of the disease were associated with lower zinc levels. The limitation of our study was small number of mucosal vitiligo that disabled us to compare this group with others.

Conclusions
Based on the results of this study, the patients with generalized vitiligo have lower zinc level. In these patients, serum zinc level is in negative correlation with patient’s age and disease duration.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

What is new?
• Patients with generalized vitiligo have lower serum zinc level.
• Lower serum zinc level in patients with vitiligo is correlated with the duration of the disease.
• There is a negative correlation between serum zinc level and age in patients with vitiligo.

References
1. Ezzedine K, Sheth V, Rodrigues M, Eleftheriadou V, Harris JE, Hamzavi IH, et al. Vitiligo is not a cosmetic disease. J Am Acad Dermatol 2015;73:883-5.
2. Yaghoobi R, Omidian M, Bagherani N. Comparison of therapeutic efficacy of topical corticosteroid and oral zinc sulfate-topical corticosteroid combination in the treatment of vitiligo patients: A clinical trial. BMC Dermatol 2011;11:7.
3. Bagherani N, Yaghoobi R, Omidian M. Hypothesis: Zinc can be effective in treatment of vitiligo. Indian J Dermatol Venereol 2011;56:480-4.
4. Ebadi A, Rad MM, Nasari S, Fesharaki RJ, Ghalamkarpour F, Younespour S, et al. The additive effect of excimer laser on non-cultured melanocyte-keratinocyte transplantation for the treatment of vitiligo: A clinical trial in an Iranian population. J Eur Acad Dermatol Venereol 2015;29:745-51.
5. Abreu AC, Duarte GG, Miranda JJ, Ramos DG, Ramos CG, Ramos MG, et al. Immunological parameters associated with vitiligo treatments: A Literature review based on clinical studies. Autoimmune Dis 2015;2015:196537.
6. Patel NS, Paghdal KV, Cohen GF. Advanced treatment modalities for vitiligo. Dermatol Surg 2012;38:381-91.
7. Kanwar AJ, Kumaran MS. Childhood vitiligo: Treatment paradigms. Indian J Dermatol 2012;57:466-74.
8. Borderé AC, Lambert J, van Geel N. Current and emerging therapy for the management of vitiligo. Clin Cosmet Investig Dermatol 2009;2:15-25.
9. Jalel A, Soumaya GS, Hamdaoui MH. Vitiligo treatment with vitamins, minerals and polyphenol supplementation. Indian J Dermatol 2009;54:357-60.
10. Mohammed GF, Gonaah AH, Al-Dhubaibi MS. Highlights in pathogenesis of vitiligo. World J Clin Cases 2015;3:221-30.
11. Cohen BE, Elbuluk N, Mu EW, Orlov SJ. Alternative systemic treatments for vitiligo: A Review. Am J Clin Dermatol 2015;16:463-74.
12. Butnaru C, Pascu M, Mircea C, Agoroaei L, Solovăstru L, Văță D, et al. Serum zinc and copper levels in some dermatological diseases. Rev Med Chir Soc Med Nat Iasi 2008;112:253-7.
13. Shameer P, Prasad PV, Kaviarasan PK. Serum zinc level in vitiligo: A case control study. Indian J Dermatol Venereol Leprol 2009;75:206-7.
14. Zeng Q, Yin J, Fan F, Chen J, Zuo C, Xiang Y, et al. Decreased copper and zinc in sera of Chinese vitiligo patients.
A meta-analysis. J Dermatol 2014;41:245-51.

15. Brüske K, Salfeld K. Zinc and its status in some dermatologic diseases – A statistical assessment. Z Hautkr 1987;62 Suppl 1:125-31.

16. Arora PN, Dhillon KS, Rajan SR, Sayal SK, Das AL. Serum zinc levels in cutaneous disorders. Med J Armed Forces India 2002;58:304-6.

17. Oiso N, Suzuki T, Fukai K, Katayama I, Kawada A. Nonsegmental vitiligo and autoimmune mechanism. Dermatol Res Pract 2011;2011:518090.

18. Zhu B, Wang J, Zhou F, Liu Y, Lai Y, Wang J, et al. Zinc depletion by TPEN induces apoptosis in human acute promyelocytic NB4 cells. Cell Physiol Biochem 2017;42:1822-36.

19. Helmy MI, Gayyar EL, Hawas S, Eissa AE. Role of oxidative stress in the pathogenesis of vitiligo. J Pan Arab Leag Dermatol 2004;15:97-105.