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Study on trace elements levels in vitiligo and normal subjects

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ABSTRACT

Introduction: Vitiligo is characterized by complete loss of ultraviolet (UV) protective pigment producing cells melanocytes. Due to the appearance of white depigmented patches causing ugly look, the disease, the through not life threatening, could be psychologically debilitating. Despite the demonstration of the presence of mild inflammatory infiltrate in the skin paralleling the loss of melanocytes, vitiligo is not an inflammatory dermatoses.
Materials and Methods: The study comprised 30 Vitiligo patients, both males and females, of age between 10-80 years. The patients were randomly selected from the outpatient clinic of Dermatology, Venereology and Leprosy Department, Narayana medical college and hospital. Cu, Zn and Se were estimated by using Atomic Absorption Spectrometry.
Results: In vitiligo patients the level of serum zinc were diminished while the level of serum copper, and selenium were increased. These changes were significantly evident in severe Vitiligo ($P<0.05$).
Conclusion: Recent studies on the role of trace elements in the etiopathogenesis and treatment of Vitiligo have shown controversial findings and are still limited. More studies are required to clarify the importance of these findings in etiopathogenesis or treatment.

1. Introduction

Vitiligo is a chronic, depigmenting skin disorder, whose pathogenesis is still unknown. Narrow band ultraviolet-B (NB-UVB) is now one of the most widely used treatment of vitiligo. It was suggested that trace elements may play a role in pathogenesis of vitiligo.[1] Although required in very small amounts, trace elements such as iron, iodine, fluoride, copper, zinc, chromium, selenium, manganese and molybdenum are vital for maintaining health.

Vitiligo is a challenging disease to treat because of its chronic nature and frequent replace. 50% of patients develop the condition by age of 20 and face social stigma. The search for newer therapeutic modalities with fewer adverse effects and autoimmune nature of the disease paved the way for use of novel topical immunomodulatory drugs and calcineurin inhibitors.[2]

Also referred to as micro minerals, these trace elements are part of enzymes, hormones and cells in the body. Insufficient intake of trace minerals can cause symptoms of nutritional deficiency. Recent studies shows that an imbalance of trace elements in the body may contribute to the pathogenesis of Vitiligo.[3]

Copper and zinc also acts as a cofactor for several enzymes especially those involved in protein & collagen synthesis. Copper is essential for the melanin production in man.[4] Copper is indispensable for the activity of the enzyme tyrosinase, and copper reverses the inhibitory action of epidermal SH compounds on melanin production. Copper and zinc deficiencies have been reported to induce hypopigmentation in various animals. Hypopigmentation of

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skin and hair results from copper deficiency in humans. This colour change is associated with the decreased activity of tyrosinase, a copper containing polyphenyl oxidase which is required for the synthesis of melanin pigment from tyrosine.[5]

Zinc is one of the important trace elements related to health and disease. Zinc is needed for the proper growth and maintenance of the human body. It is found in several systems and biological reactions and it is needed for immune function, wound healing, blood clotting, thyroid function and much more.[6] Meats, seafood, dairy products, nuts, legumes and whole grains offers relatively high levels of zinc. In humans highest concentration of zinc are found in liver, pancreas, kidneys, bones, muscles, parts of the eyes, prostate, sperms, skin, hair and nails. Zinc is found in the structure of many metalloenzymes that play an important role in protein synthesis, DNA and RNA replication and cell division. Zinc is therefore required for growth and development.

Research at the molecular levels has demonstrated deficiency of antioxidant substances in vitiliginous skin. This leads to cytotoxic action of reactive oxygen species which are generated by the ultraviolet damaged epidermis. The free radicals are also cytotoxic to melanocytes and inhibit tyrosinase.[7]

Zinc is considered as an antioxidant because the extra-cellular enzyme superoxide dismutase in zinc dependent. It plays a vital role in the protection against free radicals damage. Trace elements including zinc catalyze the rearrangement of dopachrome to form 5,6 -dhydroxy indole - 2 carboxylic acid (DICA) in the process of melanogenesis. 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.[8] 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.

Selenium is a trace elements needed for a variety of functions in the human body.[9] It acts as a cofactor for a large variety of enzyme with many functions. It is most famous for its antioxidants properties. The loss of pigmentation that occurs in vitiligo is postulated to be related to the death of melanin producing cells, which could be brought about by oxidative damages.[10]

The present study to estimate serum levels of zinc, copper and selenium levels in patients with mild, moderate and severe cases of vitiligo.

2. Materials and Methods

2.1. Patient selection

The study comprised 30 Vitiligo patients, both males and females, of age between 10-80 years. The patients were randomly selected from the outpatient clinic of Dermatology, Venereology and Leprosy Department, Narayana medical college and hospital. Cu, Zn and Se were estimated by using Atomic Absorption Spectrometry.

2.2. Inclusion criteria

All patients with Vitiligo irrespective of severity, age, sex distribution were taken into study. Exclusion criteria: patients were excluded if they had other skin disorders or received a topical or systemic treatment. Also, they are excluded if they were suffering from cardiac, diabetic, hypertension or psychiatric problems.

Complete present and past history taking including personal and family history, general examination, complete dermatologic examination, informed consent signing, and laboratory investigations (a blood sample was taken to measure the serum level of some trace elements). The concentrations of 3 elements (Zn, Cu, Se) in serum samples of psoriasis patients (n=50) were assessed in comparison with the control group(normal subjects) n=50. Statistical analysis of the data. The clinical and laboratory results obtained are statistically analyzed using SPSS/PC* (Statistical package for social science for personal computers).Student's t- test was used and data were expressed as mean $\pm$ S.D, and $P<0.05$ was considered statistically significant.

3. Results

There are three types of Vitiligo : 1.Vitiligo vulgaris 2. Segmental vitiligo 3. Generalised vitiligo. In vitiligo patients the level of serum zinc 79 μg/dL were diminished while the level of serum copper 116 μg/dL, and selenium 62 μg/ dL levels were increased. These changes were significantly evident in severe Vitiligo ($P<0.05$). Prognostic factors like Long standing disease, Leucotrichia, Acro facial lesions and Lesions on resistant areas. Vitiligo diagnosis like Age of onset, Depigmented macules with scalloped borders, Leucotrichia, Koebner's phenomenon, Predeliction to sites of trauma.

Zinc p value and statistical significance: The two-tailed P value is less than 0.0001 and By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval: The hypothetical mean is 10.0, the actual mean is 79.36, the difference between these two values is 69.36 and the 95% confidence interval of this difference: From 65.69 to 73.03.

Intermediate values used in calculations: t = 38.5378, df = 31, standard error of difference = 1.8, Mean 79.36, SD 10.18 and SEM 1.79.

Copper p value and statistical significance: The two-tailed P value is less than 0.0001 and By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval: The hypothetical mean is 14.0, the actual mean is 116.3, the difference between these two values is 102.3 and the 95% confidence interval of this difference: From 96.9 to 107.63.

Intermediate values used in calculations: t = 39.1, df = 31, standard error of difference = 2.6, Mean 116.3, SD 14.7 and SEM 2.61.

Selenium p value and statistical significance: The two-tailed P value is less than 0.0001 and By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval: The hypothetical mean is 25.0, the actual mean is 62.2, the difference between these two values is 37.28, the 95% confidence interval of this difference: From 28.2 to 46.37.

Intermediate values used in calculations: t = 8.3, df = 31 and standard error of difference = 4.4, Mean 62.2, SD 25.19 and SEM 4.45.

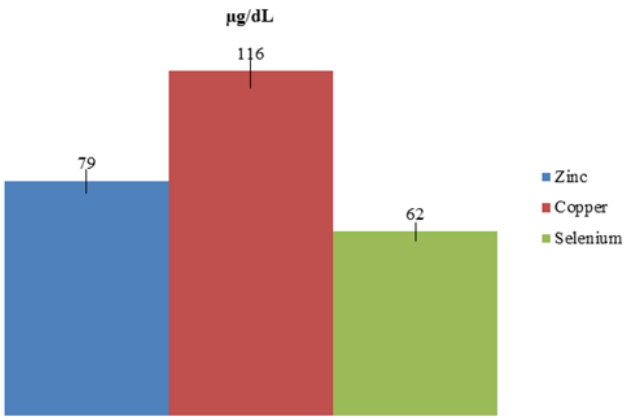

Fig. 1:

4. 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. Mirnezami M, et al[8] 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.

Zinc is known as a potential antiapoptotic agent. Apoptosis of melanocytes may be involved in the pathogenesis of vitiligo. Sharma CK, et al shows, 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.[11] They catalyse 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.

Recently, many studies have reported accumulation of free radicals (oxidative stress) in the epidermal layers of the affected skin and blood of vitiligo patients. Jain D, et al[12] Oxidative stress could be an important phenomenon leading to melanocyte death in vitiligo. Damage caused by free radicals could be a possible pathogenic factor for vitiligo. According to these results, among copper, zinc, and selenium a low serum copper concentration may play a role in premature graying of hairs in our society.

Future studies should be continued with larger sample sizes to further understand this potential relationship, in addition to looking at the role Cu supplementation may play in the treatment of vitiligo.

5. Conclusion

There is a relationship between vitiligo and serum Zn, copper and selenium. Recent studies on the role of trace elements in the etiopathogenesis and treatment of Vitiligo have shown controversial findings and are still limited. Hypopigmentation of the skin and hair results from copper deficiency in humans; the depigmentation associated with chronic excessive molybdenum intake is related to a decreased storage of copper in the liver. Copper would seem to be of prime importance because tyrosinase is a known copper-requiring enzyme. Alterations in the diet may target many of these components, and recent evidence suggests that dietary modifications and supplementation can be beneficial in the treatment of vitiligo, especially as adjuvant therapies to phototherapy or topical regimens. More studies are required to clarify the importance of these findings in etiopathogenesis or treatment.

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7. C onflict of Interest

None

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