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LEVELS OF MALONDIALDEHYDE AND ANTIOXIDANTS IN THE BLOOD OF PATIENTS WITH VITILIGO OF AGE GROUP 11–20 YEARS

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Abstract : The aetiopathogenesis of vitiligo has not been fully understood. To investigate the role of oxidative stress in pathogenesis of vitiligo, we examined the blood level of antioxidants and malondialdehyde in 40 patients with generalized vitiligo and 40 healthy volunteers belonging to same age group. Our results revealed that the level of malondialdehyde was significantly raised while those of vitamin E, uric acid and ceruloplasmin were significantly lowered ($P<0.05$) in patients with generalized vitiligo as compared to controls. This demonstrates the presence of an imbalance in the oxidant-antioxidant system in the blood of vitiligo patients and thus provides support for a free radical mediated damage as a pathogenic event in vitiligo.

Key words : free radicals malondialdehyde vitamin E uric acid ceruloplasmin antioxidants

INTRODUCTION

Vitiligo is a common and often heritable, acquired pigmentation disorder in which melanocytes in the skin, mucous membranes and the retina are destroyed (1). As a result depigmented patch appear on different parts of the body. Studies from around the world have demonstrated a high incidence (0.5 to 4%) among general population (2). This disorder affects all races and both sexes. It is primarily a disease of the young (3). Vitiligo generally appears in one of the three patterns; focal, segmental and generalised. Vitiligo is an important skin disease having major impact on quality of life of patients, many of whom experience distress and stigmatization.

Exact etiology of vitiligo is not known. Autoimmune hypothesis of vitiligo is most widely accepted since autoantibodies to melanocytes and tyrosinase have been demonstrated and also due to the association

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of vitiligo with other autoimmune diseases (4). A defective antioxidant defence is also postulated to lead to the unhindered cytotoxic action of reactive oxygen species such as superoxide anion, hydroxyl radical etc. Once formed these highly reactive free radicals can start a chain reaction and bring about lipid peroxidation producing lipid peroxides and lipoxides, whose further decomposition yields a variety of end products, including malondialdehyde (MDA). These products can cause damage to cell membrane or DNA leading to cytotoxicity, mutagenicity and cell death (5). These reactive oxygen species are generated following ultraviolet rays induced damage to the epidermis and are cytotoxic to melanocytes and also inhibit tyrosinase (6). The presence of autoantibodies to melanocytes and tyrosinase may be a secondary phenomenon to the cytokines released due to the free radical damage. To prevent free radical damage the body has a defense system of antioxidants.

The oxidative stress can either result from increase generation of free radicals or decreased destruction of these. Hence, the antioxidant plays an important role in the free radical mediated damage. The aetiology that suggests that the destruction of melanocytes in vitiligo, induced by increased oxidative stress to activate an autoimmune response seems to be appropriate. But, very few studies are available to support this. Therefore, this study was conducted to find out the balance between level of oxidative stress and antioxidant in 40 patient taking four parameters together.

MATERIAL AND METHODS

This study was undertaken in the Department of Physiology and Biochemistry, Moti Lal Nehru Medical College, Allahabad from November 2006 to November 2007. Ethical clearance from Ehical Committee of Institute was obtained for this study.

Patients and controls

Fourty patients with stable (for atleast 2 years) generalized vitiligo (involving greater than 20% body surface area symmetrically) and equal no. of healthy volunteers devoid of any depigmented patch were selected as control group in this study. The patients and controls group had males: females as 1:1 and belong to age group between 11–20 years. Patient group was chosen from Bajaj Skin Clinic and Skin Department, Swaroop Rani Nehru Hospital, Allahabad, India. They had no concomitant dermatological and/or systemic diseases and had not used any systemic or topical treatment at least for a month. There was no history of smoking, long term use of any drugs and were not doing excessive exercise except daily life activities among both the groups.

After obtaining proper consent, blood samples were collected in EDTA vials and antioxidants levels of ceruloplasmin, uric acid, vitamin E and malondialdehyde were analysed according to established methods (7–11). Statistical analyses were done by using Student's 't' test. A 'P' value less than 0.05 was considered as significant.

RESULTS AND DISCUSSION

Our result revealed a significantly higher value of malondialdehyde and lower level of uric acid, ceruloplasmin and vitamin E in

the blood of vitiligo patients as compared to controls. Malondialdehyde was higher by approximately 36% and antioxidants were lower by about 28–38% in comparision to their control. Data are presented in Table I.

Recently, many studies have reported accumulation of free radicals (oxidative stress) in the epidermal layers of the affected skin (12–14) and blood of vitiligo patients (15) 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 (16). In order to evaluate whether the activity of the disease is associated with an oxidative stress, we measured the level of oxidative stress by measuring malondialdehyde level in blood of patients with vitiligo. A measurement of malondialdehyde in the blood provides evidence of lipid peroxidation (17, 18). It is also an indirect method to detect free radical production in human. In our study the levels of malondialdehyde in the blood were found to be higher than the controls ($P<0.05$; Table I). A higher level of malondialdehyde in tissues and serum in comparision to controls were also reported in previous studies (19, 20). However, only few reports have considered the antioxidants level along with malondialdehyde that too only enzymatic antioxidants. In this study, we have considered both enzymatic and non-enzymatic antioxidants.

TABLE I: Malondialdehyde and antioxidants in vitiligo patients blood with age group 11–20 years.

Particulars	*Control Group (n=40)*	*Patient Group (n=40)*
MDA(µmoles/L)	2.333±0.84	3.184±0.87**
Vit E(mg/100 ml)	1.13±0.57	0.7±0.43*
Uric acid(mg/100 ml)	4.55±1.15	2.74±0.79**
Ceruloplasmin (mg/100 ml)	36.84±4.67	26.42±3.51**

*P<0.05, **P<0.001 as compared to control group.

Uric acid has proven to be a selective non-enzymatic and chain breaking antioxidant. It contributes as much as two-thirds of all free radical scavenging capacity in plasma. It serves a protective physiological role by preventing lipid peroxidation (21). In a variety of organs and vascular beds, local uric acid concentration increases during acute oxidative stress and ischaemia, and the increased concentrations might be a compensatory mechanism that confers protection against increased free radical activity (22). In our study level of uric acid was found to be significantly low in vitiligo patients as compared to age matched healthy controls.

Vitamin E is an enzymatic and chain breaking antioxidant and protects molecules and cell membranes in the human body against the destructive effects of oxygen containing free radicals. It plays a key role in the functioning of the immune system. A study showed high level of vitamin E in the vitiligo patient's melanocytes as compared to normal melanocytes when exposed to various concentration of a peroxidizing agent (13). However, other studies did not find significant difference of plasma vitamin E between stable and active vitiligo patients (23, 24). Significant improvement in vitiligo patients receiving antioxidant supplements containing vitamin E was seen in one study (25). In our study we found a significantly low levels of vitamin E in patients with vitiligo as compared to age matched healthy controls.

Ceruloplasmin is a transport oxidase protein with non enzymatic and preventive antioxidant property (26). A study on the antioxidant status of black patients with vitiligo, found no significant difference in the blood levels of ceruloplasmin.We found a significant difference between ceruloplasmin levels in vitiligo patients and age matched healthy controls (27).

In conclusion, a disturbance in the oxidant-antioxidant system in vitiligo patients' blood was observed in our study. This favours the aetiology that suggests that the destruction of melanocytes in vitiligo induced by increased oxidative stress and decreased level of antioxidants, activates an autoimmune response. However, the exact mechanism still needs to be analysed.

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