Testosterone and Estrogen Levels Assessment in Vitiligo Patient’s Serum

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ABSTRACT

Vitiligo is an idiopathic disorder of skin and hair characterized by melanin loss. Nonetheless thyroid disorder is a major cause of this pathology, other factors participate in its expression. Hormones such as, testosterone and estrogen have been suspected as drivers of this disorder. The present study aimed to determine the levels of testosterone and estrogen in serum of vitiligo patients. The study included 30 patients with vitiligo lesions (18 males and 12 females; ages ranged from 28–40 years and 30 healthy volunteers as control group (17 males and 13 females; ages ranged from 25-40 years). All patients of vitiligo were recruited from Medical research center of excellence of National Research Centre, Egypt, during a period of 4 months (August 2020 to November 2020). Average period of the disorder in vitiligo group was 5.0 years. Vitiligo diagnosis is done clinically and confirmed using Wood’s lamp.

Blood samples were taken from both the patient and control groups, testosterone and estrogen were assessed. Results: The present study declared a significant increase in the level of testosterone in males of VP compared to control, while significant increase in estrogen level in females of VP related to their corresponding control. Conclusion: some hormonal indicators have a role in pathogenesis of vitiligo where their disturbance leads to melanocyte destruction and/or depigmentation.

Keywords: Autoimmune disease; Melanin loss; Oxidative stress; Vitiligo; Estrogen; Testosterone

INTRODUCTION

Vitiligo is characterized by circumscribed, macules and patches of depigmentation which occurs due to distinct damage in melanocytes. It might happen at any time; patients were demonstrated as early as six weeks post labor. Its prevalence is similar in males and females, with no variance in degrees of appearance based on type of skin or race [1]. The pathogenesis of vitiligo is not well understood. There are several hypothesis about vitiligo etiology, involving autoimmune, neurohumoral, and autocytotoxic [2]. None are completely exclusive, each partially contributes. Convergence theory demonstrates that stress, infections, autoimmune diseases, mutations changing the status of the cells, and the impairment of melanocyte migration can all implicate to the pathogenesis of vitiligo [1,3].

Vitiligo is a genetic acquired disease causing morbidity among all races. Nevertheless thyroid disorder plus other factors participate in its expression. Several hormones (corticotropin-releasing hormone, α-melanocyte-stimulating hormone, testosterone, estrogen), genes (Human Leukocyte Antigen (HLA), Estrogen Receptor (ESR) 1, Vitiligo-associated protein 1 (VIT1)), and lifestyle choices (stress, diet and cosmetic products) were assumed as motivators of this disorder [4].

Factors regulating production of pigment in skin are complicated and not well-understood. The color of the skin habitually alters during pregnancy, supposing that sex steroid hormones are implicated in this event, so that estrogen elevates the production of pigment in melanocytes of human, while progesterone reduces it [5].

Estrogens may be implicated in the course of depigmentation of vitiligo as the disease’s initiation/progression is detected at pregnancy, or post contraceptives/hormonal substitution handling [6]. Immunomodulation is observed to be mediated by estrogen via alpha and beta receptors (ER α/β) of estrogen expressed on immune system cells. ERs affect function of immune system in both innate and adaptive immune response [7].

Serum levels ERβ were found to be statistically lesser in vitiligo female and male patients related to controls and also, estrogen levels were higher in patients related to controls [8]. The effect of...
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a biological 17β-estradiol on these cells showed that, estrogens can enhance the number of melanocytes in epidermis, but reduce the content of melanin and activity of tyrosinase [9].

Testosterone-mediated pigmentation is still unknown. Histologic investigation demonstrates that, testosterone and sun exposure induces melanocytes, to elevate the production of melanin. Previously Shuttleworth et al. [10] indicating the relationship between methyltestosterone and acanthosis nigricans [10]. Hence, the present study aimed to assess the serum levels of both estrogen and testosterone, as well as declaring the testosterone/estradiol ratio in vitiligo patients.

SUBJECTS AND METHODS

Subjects

Depending on Hintze [11], who found that Mean ± SD of the Testosterone (nmol/L) in control and stable vitiligo 10.42 ± 1.85 and 5.20 ± 0.81 respectively, assuming the power=0.80 and ±=0.05, by using PASS 11 release minimal sample size for an equal size a controlled clinical trial is 30 in each group.

Data are expressed as Mean ± S.D. Statistics is carried out using SPSS computer program version 22 combined with co-state computer program.

The study was carried out among 60 subjects attending the outpatient Dermatology Clinic of Medical research center of excellence, Egypt, during a period of 4 months (August 2020 to November 2020). Contributors have written an informed approval. 30 patients with vitiligo lesions (18 males and 12 females; ages ranged from 28-40 years and 30 healthy volunteers as control group (17 males and 13 females; ages ranged from 25-40 years). A general dermatological examination was performed to decide distribution, site, number, and estimated surface area of lesions for all patients. Vitiligo was diagnosed clinically (presence of white milky macules and patches and confirmed with wood's light examination). Inclusion criteria include, male and female patients with vitiligo, ages from 20 to 40 years, stable disease for 1 year, patients not suffering from other autoimmune diseases, not receiving hormonal therapy in the last 3 months, not receiving ultraviolet therapy and psoralen in the last 3 months, not receiving any topical or systemic treatments in the last 3 months. History has been recorded about age, period, progress and start of disease, precipitating factors and any preceding treatment. Blood samples were obtained from both the patient and control groups. Testosterone and estrogen levels were examined. The study protocol followed the Declaration of Medical Division, National Research Centre (NRC); all subjects were informed about the study protocol. The study was approved by Ethics Committee of NRC, Cairo, Egypt with no*19-031.

Table 1 shows that in a group of 60 subjects (30 patients and 30 controls). A study was carried out to estimate the levels of testosterone and estrogen in subjects suffering from vitiligo. A student T test was carried out for 2 independent means at P<0.05 which clarified a significant increase in levels of testosterone in male patients but no difference in female ones; however, estrogen levels showed a significant elevation in female patients rather than males which revealed no difference.

Laboratory assessment

Blood samples from patients and healthy individuals were obtained in EDTA-containing tubes and anticoagulant-free tubes. After centrifugation (3,000 g) for 10 min at 4, serum was separated in Eppendorf tubes and frozen at -80°C until analysis.

Human estradiol ELISA Core Kit and testosterone ELISA kit (Biopark, Optics Valley, and Wuhan, CHINA and ALPCO immunoasays, USA respectively) were used for measuring serum estrogen and testosterone.

RESULTS

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DISCUSSION

The vitiligo etiology is complicated and still unknown. Different hypothesis were suggested to illustrate the loss of melanocyte function [12]. As a result of the disturbances in neural and endocrinal status, other reasons involving; an autoimmune disorders, an alteration in the homeostasis of tetrahydrobiopterin (BH) [13], stressors of psychological condition [14] and defective in the defense mechanism for free radical on melanin production [15]. Schallreuter [16] revealed that keratinocytes of human synthesize and/or breakdown catecholamines. In this mechanism, tyrosine was spilt into melanin and catecholamine by tyrosine hydroxylase enzyme (signaling of neural molecules; DA, NE, etc., that regulate central and peripheral nervous systems) [17].

The present study declared significant increase in testosterone levels in male VP but not in females compared to control. While marked significant increase in estrogen levels in female VP but not in males compared to control.

In a good connection with the present results El-Sayed et al. [15], indicated that the relationship between elevated levels of catecholamine and the process of depigmentation was illustrated.
by a biochemical theory demonstrated high levels of the (6R)-l-erythro 5,6,7,8-tetrahydrobiopterin (6BH4) in epidermis of vitiligo which occurred as a consequence of enhancement in the catecholamine biosynthesis instead of melanin and formation of H2O2, which is melanocytes lethal agents resulting in autoimmune reaction. Moreover, biopterins act as inhibitors of the phenylalanine hydroxylase and tyrosinase enzymes implicated in the process of melanogenesis [18]. High levels of catecholamines cause vasoconstriction leading to hypoxia for epithelia-dermal tissue, and produce high levels of ROS (reactive oxygen species) and systemic H2O2 levels resulting from monoamine oxidation as well as their metabolites might contribute to early phase of melanocyte damage in vitiligo pateints [18,19]. Moreover, El Sayed et al. [15], illustrated that, elevated catecholamines, DA, estrogen, and prolactin levels as a consequence of hyper-H2O2 production leads either to stimulation of immune response versus melanocytes (depigmentation) or to inactivation of BH4 reductase and BH4 cofactor (reduced pigmentation), enhanced catecholamines stimulate biosynthesis of melanotan or activate its receptors. Further, the high levels of estrogen in VP might occur as a consequence of oxidative stress principally H2O2 is detected in VP skin and blood as demonstrated by Rokos et al. [20], (as detected in the existing research) which is strongly implicated in the course of depigmentation of vitiligo [21]. In addition, an important enzyme, BH4 reductase, involved in the recycling of (6R)-erythro-5,6,7,8-BH4 cofactor and was inactivated by H2O2 [22,23]. In contrast, melanoma (facial pigmentation of grayish brown color) might appear in females using oral contraceptive pills containing analogs of melanocytes. Accordingly, elevated estrogen levels in females at child-bearing age makes them less liable to vitiligo as reported by Kang and Ortonne [24].

CONCLUSION

In contrast declared the association between the lack of fertility and vitiligo, so in hypogonadism of male; the inadequate production of testosterone hormone leads to infertility. The same authors added that, the reduction in serum testosterone in males with active or stable VP results from emotional distress and low self-confidence affecting their sexual life. In conclusion current study presents a competent approach for understanding the progress of vitiligo through a trial explaining the mechanism(s) of incidence and the role of specific biomarkers contributing to its progress. Also, we indorse that any dermatologist should consider neurological, psychological, and endocrine disorders which may influence either progression or improvement of the disease.

REFERENCES