

Assessment of Prolactin Levels in Vitiligo Patients and Healthy Controls and its Association With Severity of Disease

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Abstract

Background: Vitiligo is a patchy depigmentation of skin with a prevalence of 1-2% globally, with three probable mechanisms among which immunologic affairs are most prominent. Higher blood concentrations of prolactin in autoimmune diseases like thyroiditis, rheumatoid arthritis and SLE have identified a vital role for the hormone in this regard. So we conducted the current study to evaluate serum levels of prolactin in cases of vitiligo comparing to healthy subjects to detect any relationship and responsibility of prolactin in this disease.

Methods: Through a case-control design, vitiligo sufferers referring to two university centers in Tehran were recruited beside a sex- and age-matched control group. Peripheral blood serum prolactin levels were measured to compare cases and controls in order to find any relevant changes.

Results: 110 subjects including 55 cases of vitiligo and 55 controls were evaluated but no relationship was found between serum prolactin levels and existence or severity of vitiligo.

Conclusion: Since prolactin is also produced locally in the skin, it is supposed that local release of hormone cannot hit the threshold of serum identified levels of prolactin resulting in normal concentrations in vitiligo. This study advises bigger study and measurement of prolactin in skin patches to detect lower levels of prolactin in addition to serum.

Keywords: Vitiligo; Prolactin; Serum concentration; VASI

Introduction

Vitiligo is an acquired depigmentation disorder involving around 1-2% of population worldwide disregarding age, race and gender. The sufferers are identified by selective melanocyte destruction in the skin [1]. Reduced number of melanocytes in the skin results in depigmented patches in different parts of body. Emerge mostly in second to fourth decades of life [2,3]. Despite unknown exact pathogenesis of the disease, genetics and nervous defects, neuropeptides, biochemical and auto-destructive mechanisms as well as viral infection and hormonal or cytokine interactions are blamed to be the triggers [1-4].

Prolactin, as a hormone secreted by lactotrop cells in pituitary gland, is recently seemed to have additional functions in skin biology and hair follicle growth as well [5,6]. This well-known hormone has been appreciated in several articles as an immunostimulatory factor in autoimmune disorders like psoriasis and lupus erythematosus [7-10]. Prolactin is generally found as a biomarker of disease severity in this regard. In terms of vitiligo, there are hardly a handful of researches focusing on pathophysiology and the role of hormones like prolactin. So we headed to measure serum levels of this hormone with cytokine characteristics in patients with vitiligo in comparison to healthy population.

Materials and Methods

Setting and participants

Through a prospective case-control study we recruited referrals to two central skin reference hospitals in Tehran, Iran with the main aim of comparing vitiligo patients and healthy individuals to find any difference in serum prolactin levels to conclude a role for the hormone in this matter.

Participants enrolled the case group if involved with vitiligo and the control group when have no histories or current involvement with the disease but were patients' relatives who accompanied them to the centers.

Before obtaining written informed consents, patients and controls

were visited by single dermatologist of the research to confirm the existence or absence of vitiligo. All the participants were between 18 and 60 years of age and were excluded if had any chronic hepatic disorder or immune deficiency as well as sleep disorders, brain disorders, kidney disorders, seizure, autoimmune disorders, thyroid gland diseases and of course current pregnancy or breast feeding which already changes ordinary serum hormone concentrations. Using oral contraceptives, dopamine receptors blockers, atypical antipsychotics, metoclopramide, methyl dopa, histamine antagonists, imipramine, SSRIs, calcium channel blockers and addiction were other exclusion criteria as well.

Studies showed a prevalence of 8% for hyperprolactinemia among healthy subjects which could help to explain 53 individuals for each case and control group to achieve the study power of 80% with type one error of $\alpha=0.05$. Principal investigators considered 55 cases and 55 controls for the study finally. Sex and age were matched between the groups. It means control individuals were selected considering age, sex and distributions in case group which was completed previously by census. Almost all the controls were companion of patients to the centers. Controls neither had exclusion criteria nor had vitiligo diagnosis at the time of study. All the non-menopausal female patients and controls were at the luteal phase of their menstrual period at the time of blood sampling.

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Received June 28, 2014; Accepted November 13, 2014; Published November 15, 2014

Citation: Radvar SE, Tehranchi Z, Partovikia M, Kazeminejad A, Amini SHS (2014) Assessment of Prolactin Levels in Vitiligo Patients and Healthy Controls and its Association With Severity of Disease. Pigmentary Disorders 2: 155. doi:10.4172/2376-0427.1000155

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All the participants were trained for the aims of the study and the research process as well as the value of being a part of this research to achieve a worthy target of treatment for vitiligo which has global social and mental complications and prominent stigma before starting the study. Demographics, history of disease and VASI (Vitiligo Area scoring Index) score were gathered for patients by the dermatologist.

VASI (Vitiligo Area scoring Index)

All parts of body are generally evaluated by VASI to identify vitiligo severity in patients. Hand unit and body region are the areas of VASI. Body is usually divided into five separate areas including hands, upper limbs and axillary areas, lower limbs and groins, trunk and feet. Each hand, for instance, including palmar area and fingers' volar area are considered as %1 of the whole body altogether.

Depigmentation severity is also important in VASI. The severity of depigmentation is scored between 10-100% visually or using a standard color index as follows:

- 100%: Depigmentation, no pigment is present
- 90%: Specks of pigment are present
- 75%: The depigmented area exceeds the pigmented area
- 50%: The depigmented and pigmented areas are equal
- 25%: The pigmented area exceeds the depigmented area
- 10%: Only specks of depigmentation are present

Each mentioned part of body gets a separate score and the total VASI score is finally obtained as the sum of partial scores through the following equation:

$$VASI = \Sigma (\text{all body sites}) (\text{hand units}) \times (\text{depigmentation})$$

Laboratory materials and techniques

Fasting peripheral venous blood specimens were drawn at the amount of 2 ml of each case and control individual then centrifuged for 10 minutes at 4600 rps. Supernatant serum was divided into two micro tubes to be separately stored in -40°C and -70°C before measurement of serum prolactin levels. ELISA was used to measure serum levels of the hormone.

Statistics

The power of the study was considered %80 with type one error of $\alpha=0.05$ and the confidence interval of 0.95 when the significance was 0.05. The means and other central indices were analyzed by spss20 for windows. Chi-square and t-test were used and spearman's coefficient was used in Fisher's exact test if the mentioned tests were not applicable.

Ethics

The main aims, research process and the value of findings were explained to participants before obtaining their written informed consents. Investigators kept patients' and controls' information as medical secrets. All the test fees and additional research processes were free of charge for the studied subjects.

	Categories	Cases n (%)	Controls n (%)
Sex	Male	32 (58.2)	32 (58.2)
	Female	23 (41.8)	23 (41.8)
Age	18-30	21 (38.2)	21 (38.2)
	31-40	20 (36.4)	20 (36.4)
	41-50	13 (23.6)	13 (23.6)
	>50	1 (1.8)	1 (1.8)

Table 1: Demographics including sex and age in the studied groups.

There was no conflict of interest to direct any bias in the study and all the responsible personnel were trained to do the best during the performance to get the better results in order to reduce the rate of sampling as well as fail to make subjects satisfied.

Results

As pointed out before, 110 participants including 55 cases of vitiligo and 55 healthy subjects enrolled the study, composed of 64 males and 46 females. Four age groups were introduced including 18-30, 31-40, 41-50 and older than 50 years of age. Patients were mostly in the first two groups (74.5%). Table 1 shows the demographics.

VASI mean score \pm standard deviation was 32.113 ± 9.04 in patients. The lowest score was 20 while the highest was 58. Serum prolactin as mean \pm standard deviation was $9.393 \pm 9.422 \text{ ng/ml}$ which was equal to $244.65 \pm 244.88 \text{ } \mu\text{IU/ml}$ among cases. The amounts were $9.822 \pm 5.95 \text{ ng/ml}$ and $253.78 \pm 157.01 \text{ ng/ml}$ in controls, respectively. As the Table 2 illustrates, the lowest serum prolactin was 2.9 ng/ml in cases but 3.1 ng/ml in controls. There was no significant difference found between the groups for serum prolactin levels (P value=0.776).

Although not relevant to the main aim of the study, disregarding the people groups, women had significantly higher concentrations of serum prolactin than men (P value<0.001).

Discussion

Prolactin is recently known as an immunomodulatory factor not only in cell development, especially for T and B lymphocytes, but also in dendritic cells function as suggested in vitiligo and other skin diseases. In the current study, we attempted to measure serum levels of prolactin.

We could not find any significant correlation between serum concentration of prolactin and vitiligo occurrence or its severity.

Vitiligo, as a depigmenting disorder of the skin, especially its parts where are frequently at the exposure of sunlight involves 1-8% of people, worldwide [2,11,12]. The disease has social and mental problems besides its medical complaints. Black women seem to be more in challenge with vitiligo because it's cosmetic effects on dark skins and a vast part of medical costs and burden is spent by the patients in this regard. Scleroderma, psoriasis, rheumatoid arthritis, SLE and thyroiditis are commonly studied autoimmune diseases to find immune-regulatory factors and mediators in the body [13]. Meanwhile, different pituitary hormones and body enzymes are under study to find more information

		Minimum		Maximum		Mean		SD		Sig
		Case	Control	Case	Control	Case	Control	Case	Control	
VASI		20	-	58	-	32.113	-	9.0399	-	-
Serum prolactin	ng/ml	2.9	3.1	69.40	27.40	9.39	9.82	9.42	5.95	0.775
	$\mu\text{IU/ml}$	76	10.7	1805	713	244.6	233.8	244.9	157.0	

Table 2: VASI and serum prolactin in the two groups.

on the best target of treatment in these disorders. Prolactin is one of the factors which are suggested to play role in this category of illnesses [7]. Studies have almost no debt in terms of extra pituitary sources of prolactin, particularly in the skin. The most appreciated hypothesis in vitiligo pathogenesis is immunologic one which explains destroying effect of autoantibodies on melanocytes expressing depigmented skin [14-17]. Coincidence of vitiligo with some disorders could explain the above etiology [18]. As Sawicki and colleagues suggest in concurrent cases of pernicious anemia and hypothyroidism in 2012 [15]. Some authorities have linked a list of problems to vitiligo such as stress, toxic substances, infections, genetic mutations, and interrupted melanocyte proliferation and migration [13,19-21]. Our study showed most of the vitiligo patients are in their 18-40 years of age. Males were more than females (32 vs. 23) but there is no acceptable evidence to suggest that vitiligo is more common in men based on this study.

For the first time, The European Academy of Dermatology and Venereology (EADV) evaluated serum prolactin in vitiligo patients. They found nothing to link the hormone to the disease likewise [7].

Serum prolactin and skin concentration of prolactin in psoriasis patients were measured to detect skin sources of hormone by El-Khateeb et al. [22]. The produced and released prolactin did not hit the threshold to be identified in the serum by ordinary tests but local released prolactin was found in the lesions by the investigators through this work.

Therefore we conducted the current study to evaluate prolactin level and its role in vitiligo. In the current study, we attempted to measure serum levels of prolactin to find alterations of prolactin in vitiligo patients and its correlation with severity of disease. The current study had limitations to obtain skin specimens to evaluate the biopsies to measure hormone concentration in tissue. Local prolactin in skin may be controlled by TRH and estrogen as stimulators and dopamine as central inhibitor [23].

Although the current study could not identify a correlation between prolactin and vitiligo, serum prolactin levels had wider range in case group compared to the controls.

The standard deviation was bigger in cases than in controls which could make the differences more prominent with a bigger sample size in later attempts.

Furthermore, serum prolactin concentration in controls did not exceed $27 \frac{ng}{ml}$ while it was even three times more at the higher amount among cases.

Conclusion

This study could not decline higher tissue prolactin in the skin lesion of vitiligo, as previous study detected in psoriatic plaques. This means that skin biopsies may help us detect local sources of the hormone in vitiligo like psoriasis. In addition, bigger sample size can probably show different serum prolactin levels since the hormone had wider range of change in cases than in controls.

Study Limitations

It was too hard to find cases of vitiligo who were not under treatment, especially in severe cases. This made us to extend the study duration to get enough cases of vitiligo in different ages matched with controls.

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