Angiotensin converting enzyme (ACE) gene polymorphism in vitiligo

A Thesis submitted for partial fulfillment of Doctorate Degree in Medical Biochemistry

BY

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SUMMARY

Vitiligo is a common skin disorder characterized by patterned depigmentation, because of a decrease of melanin pigment resulting from apparent melanocyte loss with profound heterogenity in its aetio-pathophysiology, and it is associated with inter-individual variation in progression of disease.

Vitiligo affects approximately 1% of the world's population. Although the exact etiology of vitiligo has not yet been established, the abnormal immune responses frequently observed in vitiligo patients have led to the suggestion that, in some cases, the condition has an autoimmune component. Autoimmune destruction of melonocytes has been proposed depending on the fact that the condition often occurs together with other autoimmune diseases and the presence of anti-melanocyte and organ specific antibodies. An increasing amount of genetic research being performed on dermatological disorders is helping to elucidate the pathogenetic mechanisms of these diseases. Polymorphisms of a number of genes which are involved in the immune system have been found to play a role in the susceptibility to vitiligo disease.

Angiotensin converting enzyme (ACE) is an important regulator of the renin-angiotensin system (RAS) and kallikrein-kininogen systems by creating angiotensin II and inactivating bradykinin. ACE gene was selected as a candidate gene as ACE plays an important role in the physiology of the vasculature, blood pressure and inflammation, and its relationship with various diseases, including autoimmune diseases, has been widely investigated.

An insertion/deletion (I/D) polymorphism of a 287-base pair (bp) sequence in intron 16 of the ACE gene accounts for the most of the variability of serum ACE activity and is associated with the development of vitiligo. The D allele appears to confer susceptibility to vitiligo.

The first aim of the present study is to detect the different genotypes of ACE gene and to study the possible association between ACE gene polymorphism and development of vitiligo. Our second aim is to estimate the high serum IL-6 and serum nitrite in vitiligo patients and to compare these factors in patients with different ACE genotypes.

The present study was conducted on 149 subjects divided into 2 groups: Group I included 74 vitiligo patients and Group II (controls) included 75 apparently healthy volunteers. A blood sample was taken for detection of ACE gene polymorphism by PCR and for detection of the level of serum IL-6 and nitrite.

Concerning statistical analysis, there was a statistically significant difference regarding IL-6 ($p<0.001$) and nitrite ($p<0.001$) between vitiligo patients and controls. Allele frequencies were significantly different between both groups (P=0.026), with the ACE I allele showing a frequency of 50% and of 63.3% in patients and controls, respectively while the ACE D allele showing a frequency of 50% and of 36.7% in patients and controls, respectively.

The analysis between the ACE genotypes groups in vitiligo patients showed statistically significant higher VIDA score (P=0.007), higher IL-6 (P=0.000) and higher nitrite (P=0.007) in patients with the DD genotype when compared to other genotypes. Multiple comparisons between the different ACE genotypes regarding the different variables showed VIDA score was significantly different only when comparing genotype II to both genotypes ID and DD, while serum IL-6 was significantly different when comparing each group to the other one, and serum nitrite was significantly different only when comparing genotype II to genotype DD.

The difference between both groups of associated stress in vitiligo patients (+ve association versus -ve association) was statistically significant as regards the percentage of disease (P=0.041) with higher % detected in patients with

associated stress. The percentage of disease was statistically significant higher in vitiligo patients with clinically universal type ($P<0.001$).

Multiple comparisons between vitiligo patients with different clinical types regarding the percentage using post hoc testing; was statistically significant higher in patients with the universal clinical type when compared to every other clinical type.

There was a significant negative correlation between VIDA score and the extent of disease in vitiligo patients and a significant positive correlation between VIDA score and serum nitrite. Also there was a significant positive correlation between serum IL-6 and nitrite in vitiligo patients.