Association of miR-146a Gene Polymorphism with Systemic Lupus Erthymatous Disease

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The present study was carried out to detect the association of microRNA-146a haplotypes polymorphisms with Systemic lupus erythematous (SLE) in Iraqi patients. PCR-SSCP technique used in present study, blood was used to DNA extraction, the results show that there was strong association between microRNA-146a and SLE in one haplotype from two. The present study concluded that there was association between microRNA-146a polymorphisms with SLE, our finding need more investigation to use this polymorphism as early indication of SLE incidence.

Keywords: Lupus , MicroRNA, miR-146a, PCR-SSCP technique, Haplotypes, Polymorphisms.

Systemic lupus erythematous is autoimmune disease lead to tissue damage due to inflammation (Lourenço. and La Cava, 2009). This disease begin with minimal or no activity and gradually increased its activity and its symptoms include skin rashes, arthralgia, and fatigue (Davies et al., 2012). It is more prevalent in female than in male with estimated ratio 9:1 (Petri et al., 2012). The factors that contribute in the etiology of the disease are environmental factors and genetic susceptibility. Viral infection or administration of certain drugs together with genetic factors can lead to promote SLE disease development (Cecarelli et al., 2015).

MicroRNAs are regulatory genes which have crucial role in regulation of the response of the innate and adaptive immunity by the post-transcriptional regulation of most genes regulatory pathways and this may lead to development of systemic autoimmunity including lupus, one of these microRNAs is miR-146a (Liang and Shen, 2012).

MATERIALS AND METHODS

1. Sample and data collection; about 2 ml of whole blood was collected from patients of Systemic lupus erythematous in Marjan hospital. All subjects in this study were taken written consent before participation in this study according to ethical approval of Iraq ministry of health, while control collected from healthy, the clinical features of disease were diagnostic by specialist prof Dr Ali al-kazaz also all data were collected for other genetic detection in this disease.

2. DNA extraction; DNA was extracted from whole blood using Favor gene extraction kit and concentration and purity were detected using nanodrope (Al-Terehi et al., 2016a).

3. MiR-146a primer was (5′-GGGTCTTTTGACCATCTCTG-3′ for the upstream primer and 5′-TCCAGTCTTCCAAGCTTTCA-3′ for downstream. (Vinci et al., 2013).

4. PCR conditions and size products MiR-146a denaturation for 5 min at 94°C, then 30 cycles (30 s at 94°C, 20 s at 57.8°C, 50 s at 72°C, and finally 10 min at 72°C). PCR products were determined by electrophoresis pattern in agarose

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Fig. 1. Electrophoresis pattern of gnomic DNA in study groups, lane 1-5 DNA from patients lane 6-10 DNA from control

Fig. 2. Electrophoresis pattern of PCR-SSCP of miR-146a gene polymorphism for patients 1, and control 2

Table 1. Haplotype frequency of miR-146a gene in patients and control

<table>
<thead>
<tr>
<th>P value</th>
<th>95 % CI</th>
<th>Odd ratio</th>
<th>patient</th>
<th>Control</th>
<th>pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.0001</td>
<td>0.0001 to 0.0280</td>
<td>0.0017</td>
<td>0%</td>
<td>75%</td>
<td>3 bandsA</td>
</tr>
<tr>
<td>&lt; 0.0001</td>
<td>35.6584 to 9932.1679</td>
<td>595.1176</td>
<td>100%</td>
<td>25%</td>
<td>2 bandsB</td>
</tr>
</tbody>
</table>

RESULTS AND DISCUSSION

The results of study show DNA extraction from whole blood (figure 1). The results of miR-146a of gene polymorphism which show in Table 1 and Figure 2 clarified the variation of haplotypes in patients and control, there were 2 pattern (A and B, ), polymorphisms show significant differences(p<0.05) between patients and control where haplotype A was appeared in control with (75% ) while in patients it was absent, and haplotype B was appeared in control with (25%...
Systemic lupus erythematosus is an autoimmune disease which causes inflammation throughout the body and this lead to trigger the innate and adaptive immune response. The study of (Boldin et al., 2011) found that mice suffering from severe lupus-like autoimmune disorder characterized by multi-organ inflammation, lymphadenopathy, splenomegaly, and greatly increased autoantibody production when they have deficient of miR-146a. MicroRNAs genes are regulatory genes which have important role in regulation and maintenance of the immune system response. MiR-146a participate in the regulation of T-cell lineage. Several studies indicated that miR-146a act on the decrease the function of interferon and toll like receptor (TLR) signaling by repressing the target genes of TLR and interferon such as (Traf6/Irak1, Stat1 and Tlr7 or Tlr9) and thus miR-146a play important role in the pathogenesis of lupus (Chan et al., 2013; So et al., 2013).

The study of (Luo et al., 2011) investigated that the genetic variant (rs57095329) in the promoter region of miR-146a in SLE patients are reduced where the risk allele G in this variant had contributing in the decrease binding to transcription factor Ets-1, and lead to reduce the levels of miR-146a in SLE patients. The meta-analysis in other study found that the SNPs (rs57095329 and rs2431697) of miR-146a are associated strongly with SLE susceptibility (Ji et al., 2014). Our finding need more investigation to detect the mutations in microRNAs that may be related with the etiology of SLE.

CONCLUSION

The present study concluded that there were one haplotype in miR-146a is associated strongly with SLE in Iraqi patients.

REFERENCES