FKBP5 polymorphism association with asthma susceptibility in asthmatic patients

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ABSTRACT

FKBP5 is FK506 binding protein 51 (component of Glucocorticoid receptor NRC3), its co-chaperone with HSP90, it regulates Glucocorticoid sensitivity and lower its affinity to cortisol hormone. FKBP5 gene overexpression reduces cortisol binding affinity and reduce GR nuclear translocation and promote nuclear translocation of non-active beta isoform of GR with FKBP5. FKBP5 encoded by FKBP5 gene, it was located on chromosome 6 p21.31, spans for 155 kb, and consists of 13 exons.

It was found FKBP5 polymorphism association with mood disorder, anxiety and psychiatric disease, increased susceptibility to major depression posttraumatic stress disorder (PTSD) also an increased the risk to suicide. The current study aimed to investigate the association FKBP5 gene polymorphism with asthma susceptibility and glucocorticoid resistant in asthmatic patients.

METHODS AND MATERIALS

case control study was conducted from March 2017 to April 2018, sixty eight asthmatic patients was enrolled in the study, while the control individuals were 40.

DNA was extracted from whole blood samples that were pulled from asthmatics and healthy control by using (DNA extraction kit GS100, Geneaid, Korea). The FKBP5 gene fragment which span from (3563943 to 3564004) on chromosome 6 21.31 exactly located in intron 2. Gene amplification by conventional polymerase chain reaction PCR was carried out by (Bioneer, Korea)

then these amplicons were sequenced by using Sanger method (Big dye terminator method) at (Macrogen company Korea) to detect the exact sequence of nucleotides (Sanger et al.,1977) and to find out the variation of this gene fragment from reference sequence.

Sequences were analyzed with online genious prime software version 2019. 1.1 and aligned by mapping on reference sequence on NCBI and SNPs were checked, genotype, allele frequency and odds ratio were calculated by using SPSS 20 Inc. Chicago, Illinois, USA.

RESULTS

The FKBP5 fragment sequencing revealed the presence of (rs1360780) and one novel SNP found just in 17 sample of asthmatic patients as compared do SNP data NCBI.

The FKBP5 variant (rs1360780) revealed allele frequency of risk allele T was (41.18 %) in patients and (20%) in control P<0.001 and O.R=2.8 when compared to wild C allele frequency (58.82 %) in patients and (64%) in control. The novel SNP FKBP5 as compared to SNP database at NCBI located at NC 000006.12, g: 35639490 in which wild T allele was substituted with G found in 17 patients, the novel SNP was submitted to clinar submission portal of NCBI with accession number rs158142263. They show asthma susceptibility risk factor with allele G frequency 11.76 % in asthmatics and 2.5 % in control OR=5.2, P <0.05 when compared to wild T allele frequency 88.24% in asthmatic and 97.5% in control.

CONCLUSIONS

The risk allele T of rs1360780 and the novel SNP rs158142283 risk allele G Predict asthma susceptibility and showed no association with corticosteroid resistant.

REFERENCES