DISERTASI

HUBUNGAN POLIMORFISME GEN DYRK IA SNP rs2154545 DAN SNP rs8132976 DAN PROTEIN TAU DENGAN RETARDASI MENTAL PADA SINDROM DOWN

Oleh
Eva Chundrayetti
NIM 07 301 033

Pembimbing

Prof. Dr. dr. Yanwirasti, PA(K)

Prof, Dr. dr. Ellyza Nasrul,SpPK(K)

Prof. Dr. Sc. Agr. Ir. Jamsari,SP,MP

PROGRAM PASCA SARJANA S3 BIOMEDIK
FAKULTAS KEDOKTERAN UNIVERSITAS ANDALAS
PADANG

2017

ABSTRAK

HUBUNGAN POLIMORFISME SNP rs2154545 DAN SNP rs8132976 GEN DYRK IA DAN PROTEIN TAU DENGAN RETARDASI MENTAL PADA SINDROM DOWN

Eva Chundrayetti

Sindrom Down (SD) atau Trisomi 21 merupakan kelainan genetic yang disebabkan abnormalitas kromosom 21 yang tidak berhasil memisahkan diri selama proses miosis sehingga terbentuk individu dengan 47 kromosom. Kelainan ini ditandai dengan adanya Retardasi Mental ringan sampai berat. Salah satu gen yang berperanan penting adalah gen DyrkIA dimana didapatkan beberapa polimorfismenya antara lain SNP rs2154545 dan SNP rs8132976. Gen DyrkIA mempengaruhi phenotip penderita dengan menghasilkan protein diantaranya protein TAU. Tujuan penelitian ini adalah membuktikan adanya polimormisme SNP rs2154545 dan SNP rs8132976 Gen DyrkIA dan Protein Tau dan menganalisis hubungannya dengan derajat retardasi mental pada Sindrom Down.

Penelitian ini bersifat observasional potong lintang dengan mengunakan sampel darah 39 orang dari murid SLB Kodya Padang, secara klinik menderita Sindrom Down dan terbukti pada pemeriksaan kariotiping pada penelitian ini 100% adalah Trisomi 21. Restriksi DNA mengunakan metode RFLP (*Restriction Fragment Length Polymorphism*). Dilakukan sekuensing dan analisa kualitatif contig, *Multple alignment* serta BLAST-NCBI untuk mengkonfirmasi hasil restriksi.

Ditemukan adanya polimorfisme SNP rs8132976 gen DyrkIA, homozygote mutan (alel AA)10.3 %,heterozigot mutan 53.8%,Wild type 35.9 % dan SNP rs2154545gen DyrkIA homozygote Mutan (alel AA) 5,1 %, heterozygote mutan 51,3%,Wild Type 43,6% dan dilakukan analisis hubungannya dengan derajat retardasi mental tidak bermakna secara statistik ($p>0,05$). Ditemukan adanya perbedaan rerata dari kadar Protein TAU pada retardasi mental derajat ringan-boderline yaitu 27438,75 pg/ml dengan kadar protein TAU derajat sedang berat 41815,65pg/ml dan terbukti hubungan yang bermakna secara statistik ($p<0,05$).

Kesimpulan dari penelitian ini ditemukan adanya mutan pada polimorfisme SNP rs8132976 dan SNP rs2154545 dan tingginya kadar protein TAU pada derajat ringan- borderline dan derajat sedang-berat Retardasi Mental.

Kata kunci: *Polymorfisme Gen Dyrk IA SNP rs2154545 dan SNP rs813297, Protein TAU,* Retardasi Mental, Down Syndrome

ABSTRACK

ASSOCIATION BETWEEN OF PHOLYMORPHISME DYRK IA GENE SNP rs2154545 AND SNP rs8132976 AND PROTEIN TAU WITH MENTAL RETARDATION IN DOWN SYNDROME

Eva Chundrayetti

Down syndrome (SD) or Trisomy 21 is a genetic disorder caused by a chromosomal abnormality of Chromosome 21 that failed to separate itself during the miosis process, than finally it cause a generation of an individual with 47 chromosomes. This disorder is characterized by mild to severe mental retardation. One of the genes that play an important role is the DyrkIA gene which consist of several polymorphisms such as SNP rs2154545 and SNP rs8132976. DyrkIA genes affect the patient phenotype by producing some proteins such as the TAU protein, afterward this proteins will influence the patient phenotype. The aim of this study was to prove the existence of SNP rs2154545 and SNP rs8132976 polymorphism of DyrkIA Genes and Protein Tau; also to analyze its relationship with the degree of mental retardation in Down syndrome.

This study was an observational cross sectional study by using blood samples of 39 students from an extraordinary school in Padang; those students were clinically suffering Down Syndrome and afterward, 100% students are proven as Trisomy 21 by using karyotyping examination. DNA restriction was performed by using Restriction Fragment Length Polymorphism (RFLP) method. Confirming the restriction results was conducted by sequencing and qualitative analysis of contig, Multple alignment and BLAST-NCBI.

This study revealed the presence of SNP rs8132976 polymorphism of Dyrk1A genes. Homogenous / mutant (AA allele) was found in 10.3% patients, heterozygot mutant in 21 (53.8%) patients, Wild Type in 14 (35.9%) patients, rs2154545gen DyrkIA homozygote Mutants (allele AA) in 5.1% patients, Heterosigot Mutant in 20 (51.3%) patients, Wild Type in 17 (43.6%) patients. Afterward, we performed a statistical analysis and found that there were no statistically significant correlation between the polymorphism and mental retardation severity ($p > 0.05$). There were average difference of TAU protein content in mild-boderline mental retardation with the TAU protein content ini moderate-severe mental retardation, the TAU level was 27438,75 pg/ml and 41815,65 pg/ml respectively; but this result was statistically significant ($p < 0,05$).

The conclusions of this study is the presence of mutants in polymorphism SNP rs8132976 and SNP rs2154545; also we found high levels of TAU protein at mild-borderline and moderate-severe degrees Mental Retardation in Down Syndrome patients.

Keyword : Polymorphism Gen Dyrk IA SNP rs2154545 and SNP rs8132976, TAU protein, Mental Retardation, Down Syndrome