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SAIPHON POLDEE: POLYMORPHISMS AND MUTATIONS OF APOLIPOPROTEIN B AND APOLIPOPROTEIN E GENE IN THAI SUBJECTS. THESIS ADVISORS: ATIP LIKIDLILID M.Sc., KLAI-UPSORN PONGRAPEEPORN Ph.D., NEDNAPIS TIRAWANCHAI Ph.D. 183 p. ISBN 974-663-909-9

To study the impact of apolipoprotein B and E polymorphisms and mutations on plasma lipid levels, the 171 subjects were obtained from Dyslipoproteinemia Clinic at Siriraj Hospital. The study of exon 1 in apolipoprotein (apo) B signal peptide insertion (I)/ deletion (D) polymorphism by PCR in 171 Thai population has shown that the allele frequencies of I and D were 0.78 and 0.22, respectively. The Thai population was subdivided into 103 hyperlipidemia, and 68 normolipidemia groups. The D allele frequencies in hyperlipidemia (I=0.74, D=0.26) was significantly higher than that in normalipidemia (I=0.83, D =0.17) ($p < 0.05$). Comparison of these allele frequencies with those reported for several other population samples showed that the Caucasian populations were significantly higher in D allele frequencies but similar in Asian populations. To detect point mutation in exon 26 of apo B-100 by PCR-RFLP in Thai population, the Arg3500Gln and Arg3531Cys were not identified in 171 Thai samples. However, the heterozygotes of Arg3611Gln were identified in 2 hyperlipidemic subjects which showed no significant reduction on lipid profiles after treatment with lipid-lowering drugs. The apo E polymorphisms were also studied by PCR-RFLP and found that the apo E2, E3, and E4 allele frequencies were 0.08, 0.80, and 0.12, respectively. Comparison of these allele frequencies between the hyperlipidemia (E2=0.08, E3=0.76, E4=0.16) and normolipidemia (E2=0.08, E3=0.85, E4= 0.07) showed that the E4 allele frequencies were significantly higher by an increase of 86% than that of normolipidemia ($p<0.05$). We also compared these allele frequencies with those reported for several other population samples. The results showed that there were marked significant differences in Thai and other racial populations, e.g. Finnish, Sudanese, Swedish, Trinidadian and Greenlander ($p<0.05$). These differences in apo E allele frequencies appeared to be mainly due to differences of an increased E4 allele frequencies in Finnish, Sudanese, and Swedish. The difference of Trinidadian from Thai populations was due to an increase in apo E2 allele frequency (60%) whereas there was a decrease (70%) in the Greenlander population. From the study of the relationship between apo B Ins/Del polymorphism and lipid profiles in plasma, the results showed that significant differences of these polymorphisms and lipid profiles were observed in only ID genotypes of hyperlipidaemia. These significant differences may be due to the influence of exacerbating factors which is particularly strong in old age. However, comparison between before and after treatment with lipid-lowering drugs for 3-5 years showed that II and ID genotypes significantly decreased TC and LDL-C after treatment. ($p<0.001$). DD genotypes showed no decreased in plasma lipids. The association of apo E polymorphism and plasma lipid profiles showed that the E4 allele was associated with the higher levels of TC and LDL-C ($p<0.05$) whereas E2 allele was associated with a higher level of TG ($p<0.001$) as compared with the normal E3. We also compared the effects of lipid-lowering drugs before and after treatment on plasma lipid levels in individuals with various apo E polymorphisms. The results showed that only homozygous E3/E3 significantly reduced TC, LDL-C, and TG after treatment for 3-5 years, (TC, LDL-C; $p<0.001$; TG; $p<0.01$). The genotypes containing E4 allele showed significantly decreased TC and LDL-C levels ($p<0.05$). The genotype containing E2 allele showed no significant differences of lipid levels before and after treatment.