

CNDP1, NOS3, and MnSOD polymorphisms as risk factors for diabetic nephropathy among type 2 diabetic patients in Malaysia

ABSTRACT

Type 2 diabetes mellitus (T2DM) is associated with a high incidence of nephropathy. The aim of this study was to investigate the association of a genetic polymorphism of carnosinase (CNDP1-D18S880 and -rs2346061), endothelial nitric oxide synthase (NOS3-rs1799983), and manganese superoxide dismutase (MnSOD-rs4880) genes with the development of diabetic nephropathy among Malaysian type 2 diabetic patients. A case-control association study was performed using 652 T2DM patients comprising 227 Malays (without nephropathy = 96 and nephropathy = 131), 203 Chinese (without nephropathy = 95 and nephropathy = 108), and 222 Indians (without nephropathy = 136 and nephropathy = 86). DNA sequencing was performed for the D18S880 of CNDP1, while the rest were tested using DNA Sequenom MassARRAY to identify the polymorphisms. DNA was extracted from the secondary blood samples taken from the T2DM patients. The alleles and genotypes were tested using four genetic models, and the best mode of inheritance was chosen based on the least value. The rs2346061 of CNDP1 was significantly associated with diabetic nephropathy among the Indians only with OR = 1.94 and 95% CI = (1.76–3.20) and fitted best the multiplicative model, while D18S880 was associated among all the three major races with the Malays having the strongest association with OR = 2.46 and 95% CI = (1.48–4.10), Chinese with OR = 2.26 and 95% CI = (1.34–3.83), and Indians with OR = 1.77 and 95% CI = (1.18–2.65) in the genotypic multiplicative model. The best mode of inheritance for both MnSOD and NOS3 was the additive model. For MnSOD-rs4880, the Chinese had OR = 2.8 and 95% CI = (0.53–14.94), Indians had OR = 2.4 and 95% CI = (0.69–2.84), and Malays had OR = 2.16 and 95% CI = (0.54–8.65), while for NOS3-rs1799983, the Indians had the highest risk with OR = 3.16 and 95% CI = (0.52–17.56), followed by the Chinese with OR = 3.55 and 95% CI = (0.36–35.03) and the Malays with OR = 2.89 and 95% CI = (0.29–28.32). The four oxidative stress-related polymorphisms have significant effects on the development of nephropathy in type 2 diabetes patients. The genes may, therefore, be considered as risk factors for Malaysian subjects who are predisposed to T2DM nephropathy.