

INTISARI

POLIMORFISME K121Q GEN *ECTONUCLEOTIDE PYROPHOSPHATASE PHOSPHODIESTERASE 1* (ENPP1) SEBAGAI FAKTOR RISIKO RESISTENSI INSULIN PADA INDIVIDU OBESITAS

Latar Belakang Prevalensi obesitas di Indonesia pada tahun 2013 sebesar 15.4%. Obesitas menjadi masalah kesehatan penting karena dapat menjadi faktor risiko bagi penyakit lainnya. Resistensi insulin merupakan sindrom metabolik yang sering terjadi akibat obesitas. Gen ENPP1 dilaporkan berkaitan dengan terjadinya obesitas dan resistensi insulin. Polimorfisme K121Q gen ENPP1 diketahui memiliki hubungan dengan obesitas dan resistensi insulin di berbagai populasi, namun beberapa hasil penelitian lainnya masih kontroversial. Penelitian *in vitro* menunjukkan bahwa alel C (varian glutamin) dapat berikatan tiga kali lebih kuat dibandingkan dengan alel A (varian lisin). Hasil beberapa penelitian sebelumnya yang masih kontroversial menyebabkan penelitian mengenai hubungan polimorfisme K121Q gen ENPP1 dengan obesitas dan resistensi insulin menarik untuk diteliti.

Tujuan Mengkaji hubungan polimorfisme K121Q gen ENPP1 sebagai faktor risiko resistensi insulin pada individu obesitas populasi Jawa.

Metode Penelitian ini merupakan studi kasus-kontrol. Individu obesitas dengan $IMT > 25 \text{ kg/m}^2$ masuk kelompok kasus dan individu normal dengan $IMT 18-23 \text{ kg/m}^2$ masuk kelompok kontrol. Pengambilan darah dilakukan setelah subjek puasa minimal 8 jam dan darah ditampung pada tabung berisi EDTA. Plasma-EDTA digunakan untuk pengukuran glukosa darah puasa dan insulin puasa. Glukosa darah puasa diukur menggunakan metode GOD-PAP. Insulin puasa diukur menggunakan metode ELISA. Analisis genotip dilakukan dengan metode PCR-RFLP dan visualisasi hasil restriksi menggunakan metode elektroforesis pada gel agarose 2%.

Hasil Genotip AC lebih banyak ditemukan pada kelompok kasus dibandingkan dengan kelompok kontrol. Pembawa genotip AC memiliki risiko obesitas lebih tinggi namun secara statistik tidak berbeda signifikan (OR 1.658; 95% CI 0.6-4.5). Kadar glukosa puasa, insulin puasa, dan HOMA-IR ditemukan lebih tinggi pada pembawa AC. Individu obesitas dengan genotip AC memiliki risiko resistensi insulin lebih tinggi dan hasil ini signifikan secara statistik (OR 6.62; 95% CI 1.3-34.5; $p=0.025$).

Kesimpulan Terdapat hubungan antara polimorfisme K121Q gen ENPP1 dengan resistensi insulin pada individu obesitas populasi Jawa.

Kata Kunci Obesitas, Resistensi Insulin, ENPP1, Polimorfisme K121Q

ABSTRACT

K121Q POLYMORPHISM OF ECTONUCLEOTIDE PYROPHOSPHATASE PHOSPHODIESTERASE 1 (ENPP1) GENE AS RISK FACTOR OF INSULIN RESISTANCE IN OBESE ADULTS

Introduction Prevalence of obesity in Indonesia was 15.4% in 2013. Obesity becomes one of important health problem because it might be a risk factor for other diseases or metabolic syndromes. Insulin resistance is the most common metabolic syndrome related to obesity. Previous study reported ENPP1 gene was associated with obesity and insulin resistance. Some studies on different population and ethnic reported that K121Q polymorphism of ENPP1 gene was associated with obesity and insulin resistance, but other studies reported controversial result. Study in vitro showed that C allele (glutamine variant) bound to insulin receptor three folds stronger than A allele (lysine variant). The association of K121Q polymorphism of ENPP1 gene remains controversial so this study becomes interesting to be performed.

Aim of Research To investigate the association of K121Q polymorphism of ENPP1 gene as risk factor of insulin resistance in Javanese obese adults

Methods This is a case-control study. Obese adults with BMI > 25 kg/m² were included to case group and adults with BMI 18-23 kg/m² were included to control group. Blood samples were collected after 8 hours fasting. Plasma-EDTA was used to measure fasting blood glucose and fasting insulin. Blood glucose was measured by using GOD-PAP method. Fasting insulin was measured by ELISA method. Genotype analysis was performed by PCR-RFLP and restriction by *AvaII* was visualized by electrophoresis on agarose gel 2%.

Result Genotype AC was found higher in case group compared to control group. The risk of obesity was higher in individuals carried AC but statistically not significant (OR 1.658; 95% CI 0.6-4.5). Polymorphism of K121Q ENPP1 gene was associated with the increasing of fasting blood glucose, fasting insulin, and HOMA-IR. Obese adults with genotype AC has higher risk of insulin resistance and this result is statistically significant (OR 6.6295% CI 1.3-34.5; $p=0.025$).

Conclusion There is an association between K121Q polymorphism of ENPP1 gene with insulin resistance in Javanese obese adults.

Key Words Obesity, Insulin resistance, ENPP1, K121Q polymorphism