

INTISARI

Hipertensi masih menjadi masalah utama dalam dunia kesehatan. Prevalensi hipertensi di Indonesia terus meningkat hingga saat ini mencapai 34,11%. Penggunaan antihipertensi golongan *Angiotensin Converting Enzyme inhibitor* (ACEi) seperti kaptopril sebagai salah satu lini pertama antihipertensi memiliki respon klinis yang bervariasi. Berbagai penelitian telah mengaitkan alel T dari *Single Nucleotide Polymorphism* (SNP) gen *AGT* rs699 dengan peningkatan kadar angiotensinogen dalam plasma sehingga mempengaruhi respon ACEi. Penelitian ini bertujuan untuk mengkaji distribusi frekuensi SNP *AGT* rs699 dan pengaruhnya terhadap efektivitas terapi kaptopril pada pasien hipertensi di Indonesia.

Total 142 pasien hipertensi pengguna kaptopril di Yogyakarta dan Bali dilibatkan dalam penelitian *case-control* ini. DNA diisolasi dari sampel darah 69 pasien yang mencapai target tekanan darah (kelompok kontrol) dan 73 pasien yang tidak mencapai target tekanan darah (kelompok kasus). SNP *AGT* rs699 diidentifikasi menggunakan metode *Polymerase Chain Reaction - Restriction Fragment Length Polymorphism* (PCR-RFLP) dan visualisasi menggunakan elektroforesis gel agarose. *Hardy-Weinberg Equilibrium* (HWE) digunakan untuk menghitung proporsi frekuensi alel. Analisis dengan uji *Chi square* untuk membandingkan frekuensi genotip antara kedua kelompok. Hubungan antara SNP *AGT* rs699 dengan efektivitas terapi ACEi dianalisis dengan perhitungan *Odds Ratio* (OR) dengan *Confidence Interval* (CI) 95%.

Distribusi frekuensi genotip seluruhan pasien hipertensi yaitu MM (10,56%); MT (32,39%); TT (57,04%). Frekuensi genotip berbeda signifikan ($p < 0,05$) antara kelompok kontrol MM (17,39%); MT (42,03%); TT 40,58% dan kelompok kasus MM (4,11%); MT (23,29%); TT (72,60%). Distribusi frekuensi alel seluruh pasien yaitu M (0,27); T (0,73). Frekuensi alel kelompok kontrol yaitu M (0,38); T (0,62) dan kelompok kasus M (0,16); T (0,84). Pasien hipertensi pengguna kaptopril yang membawa genotip MM (OR= 4,90; CI= 1,322-18,253) atau alel M (OR= 3,8; CI= 1,919-7,844) memiliki kecenderungan untuk mencapai target tekanan darah lebih baik dibandingkan genotip dan alel lainnya ($p < 0,05$). Dapat disimpulkan bahwa kehadiran alel T dari SNP *AGT* rs699 mempengaruhi terapi kaptopril menjadi kurang efektif.

Kata Kunci: Hipertensi, *Single Nucleotide Polymorphism*, gen angiotensinogen (*AGT*), rs699, kaptopril.

ABSTRACT

Hypertension is still a major problem in the world of health. The prevalence of hypertension in Indonesia continues to increase and currently reaches 34.11%. The use of Angiotensin Converting Enzyme inhibitor (ACEi) antihypertensives such as captopril as a first-line antihypertensive has varied clinical responses. Various studies have suggested the T allele of the Single Nucleotide Polymorphism (SNP) AGT rs699 gene with increased levels of angiotensinogen in plasma thereby affecting the ACEi response. This study aims to examine the frequency distribution of SNP AGT rs699 and its influence on the effectiveness of captopril therapy in hypertensive patients in Indonesia.

A total of 142 hypertensive patients using captopril in Yogyakarta and Bali were involved in this case-control study. DNA isolation was carried out on blood samples from 69 patients who reached the blood pressure target (control group) and 73 patients who did not reach the blood pressure target (case group). SNP AGT rs699 was identified using the Polymerase Chain Reaction - Restriction Fragment length Polymorphism (PCR-RFLP) method and visualization using agarose gel electrophoresis. Hardy-Weinberg Equilibrium (HWE) was used to calculate the proportion of allele frequencies. Analysis using Chi square test to compare genotype frequencies between the two groups. The relationship between SNP AGT rs699 and the effectiveness of ACEi therapy was explained by calculating the Odds Ratio (OR) with a 95% Confidence Interval (CI).

Genotype frequency distribution of hypertensive patients is MM (10.56%); MT (32.39%); TT (57.04%). The genotype frequencies were significantly different ($p < 0.05$) between control group MM (17.39%); MT (42.03%); TT 40.58% and case group MM (4.11%); MT (23.29%); TT (72.60%). The allele frequency distribution for all patients is M (0.27); T (0.73). The allele frequency of the control group was M (0.38); T (0.62) and case group M (0.16); T (0.84). Hypertensive patients using captopril who carry the MM genotype (OR= 4.90; CI= 1.322-18.253) or the M allele (OR= 3.8; CI= 1.919-7.844) have a tendency to achieve blood pressure targets better than the other genotype and allele ($p < 0.05$). It can be concluded that the presence of the T allele of SNP AGT rs699 makes captopril therapy ineffective.

Keywords: Hypertension, *Single Nucleotide Polymorphism*, angiotensinogen gene (AGT), rs699, captopril.