

## ABSTRACT

Asthma is a respiratory disease that occurs in children and adults, both men and women. Several classes of drugs indicated for asthma include  $\beta_2$  agonists, but the effectiveness and side effects that may appear vary widely among individuals. Among differences in effectiveness and side effects are genetic factors, particularly receptor genes. This study was conducted to assess the polymorphism of the  $\beta_2$ -adrenergic receptor (ADRB2) gene against the effectiveness and side effects of  $\beta_2$ -Agonist in asthma as well as frequency distribution of Arg16Gly and Gln27Glu gene polymorphisms. This was an observational study using cross sectional design conducted in six hospitals in Yogyakarta Special Region and one hospital in Central Java for 14 months, between June 2015 and August 2016. The subjects of the study were asthma patients who underwent treatment at the hospital's polyclinic who met the inclusion and exclusion criteria and were willing to participate in the study by signing a consent statement. The effectiveness was assessed based on the value of asthma control using the Asthma Control Test (ACT) questionnaire. Side effects were seen from the side effect questionnaire followed by an analysis of adverse events occurring using the Naranjo scale. Polymorphism was performed using a patient's blood sample, followed by DNA isolation, and ended with gene identification. The total of 101 patients, based on the frequency of Arg16Gly gene distribution (rs 1042713) consisted of 74.26% Arg16Arg (Wildtype); 9.90% Gly16Gly (mutant); 15.84% Arg16Gly (Heterozygot). Frequency distribution of the gene Gln27Glu (rs1042714) consists of 64.36% Gln27Gln (Wildtype); 7.92% Glu27Glu (mutants); 27,72% Gln27Glu (Heterozygot). There is no effect of Arg16Gly gene polymorphism (rs 1042713) and Gln27Glu (rs 1042714) on the effectiveness of  $\beta_2$  agonists ( $p > 0.05$ ). There is an influence of Arg16Gly gene polymorphism (rs 1042713) and Gln27Glu (rs 1042714) on the incidence of  $\beta_2$  agonist side effects ( $p < 0.05$ ).

**Keywords:** Asthma, ADRB2 Genes, Agonis- $\beta_2$ , Effectiveness, Side Effects.

## INTISARI

Asma merupakan penyakit saluran pernafasan yang dialami anak dan dewasa, laki-laki maupun perempuan. Beberapa golongan obat diindikasikan untuk asma termasuk agonis  $\beta_2$ , tetapi efektivitas maupun efek samping yang mungkin muncul sangat bervariasi antar individu. Diantara perbedaan efektivitas dan efek samping adalah faktor genetik, khususnya gen reseptor. Penelitian ini dilakukan untuk mengkaji polimorfisme gen  $\beta_2$ -adrenergic receptor (ADRB2) terhadap efektivitas dan efek samping  $\beta_2$ -Agonis pada penderita asma serta frekuensi distribusi polimorfisme gen Arg16Gly dan Gln27Glu. Penelitian ini merupakan penelitian observasional menggunakan rancangan potong lintang yang dilakukan di enam rumah sakit di Daerah Istimewa Yogyakarta dan satu rumah sakit di Jawa Tengah selama 14 bulan, yaitu antara bulan Juni 2015 sampai Agustus 2016. Subjek penelitian adalah pasien asma yang menjalani pengobatan di poliklinik penyakit dalam rumah sakit tersebut yang memenuhi kriteria inklusi dan eksklusi serta bersedia ikut dalam penelitian dengan menandatangani surat pernyataan persetujuan. Efektivitas dinilai berdasar nilai kontrol asma menggunakan kuesioner *Asthma Control Test* (ACT). Efek samping dilihat dari kuesioner efek samping yang dilanjutkan dengan analisis kejadian efek samping menggunakan skala Naranjo. Polimorfisme dilakukan dengan menggunakan sampel darah pasien, dilanjutkan isolasi DNA, dan diakhiri dengan identifikasi gen. Total pasien sebanyak 101, berdasar frekuensi distribusi gen Arg16Gly (rs 1042713) terdiri atas 74,26% Arg16Arg (*Wildtype*); 9,90% Gly16Gly (*mutant*); 15,84% Arg16Gly (*Heterozygot*). Frekuensi distribusi gen Gln27Glu (rs1042714) terdiri atas 64,36% Gln27Gln (*Wildtype*); 7,92% Glu27Glu (*Mutan*); 27,72% Gln27Glu (*Heterozygot*). Tidak ada pengaruh polimorfisme gen Arg16Gly (rs 1042713) dan Gln27Glu (rs 1042714) terhadap efektivitas agonis  $\beta_2$  ( $p > 0,05$ ). Ada pengaruh polimorfisme gen Arg16Gly (rs 1042713) dan Gln27Glu (rs 1042714) terhadap kejadian efek samping agonis  $\beta_2$  ( $p < 0,05$ ).

Kata kunci: Asma, Gen ADRB2, Agonis- $\beta_2$ , Efektivitas, Efek samping.