

Hubungan Polimorfisme Gen HMOX1rs2071746 (-413A>T) dan Microsatellite (GT)n Pada Pasien Hipertensi Arteri Pulmonal (HAP) Terkait Defek Septum Atrium Pada Suku Jawa

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Intisari

Latar Belakang: Hipertensi arteri pulmonal (HAP) merupakan komplikasi serius pada pasien dengan defek septum atrium (DSA), yang diduga berkaitan dengan stres oksidatif dan disfungsi endotel. Gen heme oxygenase-1 (HO-1) memiliki peran protektif terhadap kerusakan vaskular melalui aktivitas antioksidan. Variasi genetik seperti SNP rs2071746 dan (GT)n *repeat polymorphism* pada promotor HO-1 diketahui mempengaruhi ekspresi HO-1.

Tujuan: Mengidentifikasi hubungan antara polimorfisme gen HO-1 (rs2071746 dan (GT)n), kadar HO-1 plasma, serta produk metaboliknya (bilirubin, karboksihemoglobin/HbCO, dan feritin) terhadap risiko HAP pada pasien DSA.

Metode: Penelitian ini menggunakan desain observasional analitik *cross-sectional*. Subjek adalah 51 pasien DSA dengan HAP dan 50 pasien dengan hipertensi pulmonal atau tanpa hipertensi pulmonal. Pemeriksaan meliputi genotipe HO-1, kadar HO-1 plasma, bilirubin, HbCO, feritin, dan Endothelin-1 (ET-1). Analisis statistik dilakukan menggunakan uji *Kruskal-Wallis*, *Chi-square*, *Spearman*, *Mann Whitney* dan regresi logistik.

Hasil: alel T dan L pada polimorfisme HMOX1 berhubungan signifikan dengan peningkatan risiko HAP. Kadar HO-1 plasma lebih rendah dan ET-1 lebih tinggi pada kelompok HAP ($p < 0,05$). Tidak ditemukan perbedaan signifikan kadar bilirubin dan HbCO antara kelompok HAP dan non- HAP, namun feritin menunjukkan perbedaan yang signifikan antar kelompok.

Kesimpulan: Polimorfisme HO-1 rs2071746 berperan terhadap risiko HAP pada pasien DSA. Aktivitas HO-1 yang lebih rendah mungkin memfasilitasi perkembangan HAP melalui jalur stres oksidatif dan disfungsi endotel. Temuan ini mendukung potensi HO-1 sebagai biomarker risiko dan target terapi molekuler.

Kata kunci: hipertensi arterial pulmonal, defek septum atrial, heme oxygenase-1, polimorfisme, suku Jawa

Association of HMOX1 Gene rs2071746 (-413A>T) and Microsatellite (GT)n Polymorphisms with Pulmonary Arterial Hypertension in Atrial Septal Defect Patients of Javanese

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Abstract

Background: *Pulmonary arterial hypertension (PAH) is a severe complication in patients with atrial septal defect (ASD), potentially linked to oxidative stress and endothelial dysfunction. The heme oxygenase-1 (HO-1) gene plays a protective role against vascular damage through its antioxidant effects. Genetic variations such as SNP rs2071746 and (GT)n repeat polymorphisms in the HO-1 promoter are known to influence HO-1 expression.*

Objective: *To evaluate the association between HO-1 gene polymorphisms (rs2071746 and (GT)n), plasma HO-1 levels, and its metabolic products (bilirubin, carboxyhemoglobin/COHb, and ferritin) with the risk of PAH in ASD patients.*

Methods: *This was an observational analytic study with a cross-sectional design. Subjects were 51 patients ASD PAH patients and 50 patients with pulmonary hypertension or without pulmonary hypertension. Genotyping of HO-1, plasma HO-1, bilirubin, HbCO, ferritin, and Endothelin-1 (ET-1) levels were analyzed. Statistical tests included Kruskal-Wallis, Chi-square, Spearman, Mann Whitney and logistic regression.*

Results: *The allele T and L of HMOX1 were significantly associated with increased PAH risk. Plasma HO-1 levels were lower and ET-1 levels were higher in the PAH group ($p < 0.05$). No significant differences were found in bilirubin and COHb levels between PAH and non-PAH groups, meanwhile ferritin showed significant difference between groups.*

Conclusion: *HO-1 rs2071746 polymorphisms contribute to PAH susceptibility in ASD patients. Reduced HO-1 activity may facilitate PAH development through oxidative stress and endothelial dysfunction. These findings highlight the potential of HO-1 as a genetic risk marker and therapeutic target.*

Keywords: *Pulmonary arterial hypertension, Atrial septal defect, Heme oxygenase-1, Polymorphism, Javanese population*