Peran Mutasi Regio NS5A Virus Hepatitis C dan SNP IL-28B Pejamu terhadap Keberhasilan Terapi Pegylated Interferon dan Ribavirin pada Pasien Koinfeksi VHC-HIV = The Role of Mutation of Hepatitis C Virus NS5A Region and SNP IL-28B of Host toward The Successfulness of Pegylated Interferon and Ribavirin Treatment Among Patients with HCV-HIV Co-Infection

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Abstrak

HIV coinfection in HCV-infected patients accelerates the course of disease and affects the outcome of Peg-IFN/RBV combination treatment. HCV-HIV coinfected patients are suspected to have HCV mutation in NS5A-ISDR/PKR-BD region that had a role to the successfulness of Peg-IFN/RBV therapy. SNP IL-28B polymorphism is predicted to have an effect on the HCV quasi-species evolution. However, until now the effect of HCV NS5A mutation and SNP IL-28B of the host to the response of treatment is still unclear.

This study aimed to determine the presence and role of HCV NS5A-ISDR/PKR-BD region mutation and host SNP IL-28B on the succes of Peg-IFN/RBV combination treatment in HCV-HIV coinfected patients.

Prospective cohort study design was conducted in this study. Plasma sample was collected from 22 monoinfected and 134 HCV-HIV coinfected patients prior to therapy. All of them were treated with Peg-IFN/RBV for 48 weeks. The examination of HCV RNA was performed 24 weeks after the end of therapy. PCR nucleotide sequencing was performed after the RNA virus extraction and cDNA synthesis had been performed. Analysis of secondary structure and prediction of mutation function were assessed by PredictProtein (PP) program.

Sixteen from thirthy HCV-HIV co-infection patients and none from eight HCV patients achieved SVR. Nonneutral mutation 1 was found in 23/30 subjects with HCV-HIV co-infection. The presence of nonneutral mutation 1 was observed more frequent in SVR group than non-SVR group. Nonneutral mutation 1 was associated with SVR achievement, regardless the monoinfection or coinfection status (p = 0.04). Interaction of CC gene and nonneutral mutation was not associated with SVR. Secondary structure transformation of VHC NS5A was not associated with SVR in coinfected subjects. NS5A binding site structure was different from consensus in SVR group, while the structure was similar to consensus in non-SVR group.

Nonneutral mutation 1 has the most important role on the SVR achievement in patients treated with Peg-IFN/RBV. The interaction of CC-gene and nonneutral mutation was not associated with SVR. The change of secondary structure was also not associated with SVR achievement, however, the changes of NS5A binding site structure were found in HCV-HIV coinfected patients who achieved SVR.
<hr>Koinfeksi HIV pada pasien dengan infeksi VHC dapat memperberat perjalanan penyakit dan memengaruhi keberhasilan terapi kombinasi Peg-IFN/RBV. Pasien koinfeksi VHC-HIV diduga mengalami

mutasi VHC pada regio NS5A-ISDR/PKR-BD yang mempunyai peran terhadap keberhasilan terapi Peg-IFN/RBV. Polimorfisme SNP IL-28B diprediksi berpengaruh terhadap evolusi quasi-spesies VHC, namun hingga saat ini keberadaan dan peran mutasi VHC NS5A serta SNP IL-28B pejamu pada koinfeksi VHC-HIV terhadap keberhasilan terapi masih belum diketahui secara jelas.

Penelitian ini bertujuan untuk mengetahui keberadaan dan peran mutasi VHC NS5A-ISDR/PKR-BD serta SNP IL-28B pejamu terhadap keberhasilan terapi dengan kombinasi Peg-IFN/RBV pada pasien koinfeksi VHC-HIV.

Penelitian ini menggunakan desain studi kohort prospektif. Sampel plasma dikumpulkan dari 22 subjek monoinfeksi dan 134 subjek koinfeksi sebelum menjalani terapi. Seluruh pasien mendapatkan terapi Peg-IFN/RBV selama 48 minggu. Pemeriksaan VHC RNA setelah 24 minggu dari akhir terapi dilakukan untuk menilai respons terapi (sustained virological response/SVR 24). Sekuensing nukleotida menggunakan PCR dilakukan setelah ekstraksi RNA virus dan sintesis cDNA dari sampel plasma. Analisis struktur sekunder dan prediksi fungsi mutasi menggunakan program PredictProtein (PP).

Sebanyak 16 pasien dari 30 pasien koinfeksi VHC-HIV yang mengalami SVR serta tidak ada dari 8 pasien monoinfeksi VHC yang mengalami SVR. Mutasi nonnetral 1 ditemukan pada 23/30 pasien koinfeksi VHC-HIV. Keberadaan mutasi nonnetral 1 didapatkan lebih tinggi pada kelompok SVR (14 pasien) dibandingkan dengan non-SVR (9 pasien). Mutasi nonnetral 1 berhubungan dengan kejadian SVR, tanpa memandang status monoinfeksi dan koinfeksi ($p = 0,04$). Interaksi antara gen CC dan mutasi nonnetral tidak berhubungan dengan SVR. Perubahan struktur sekunder NS5A tidak berhubungan dengan SVR pada pasien koinfeksi. Struktur binding site NS5A pada kelompok SVR didapatkan berbeda dengan konsensus, sedangkan pada kelompok non-SVR mirip dengan konsensus.

Mutasi nonnetral 1 berperan terhadap kejadian SVR pada pasien yang mendapat terapi Peg-IFN/RBV. Interaksi mutasi nonnetral dan gen CC tidak berhubungan dengan pencapaian SVR. Perubahan struktur sekunder juga tidak berhubungan dengan pencapaian SVR, akan tetapi perubahan struktur binding site NS5A-ISDR/PKR-BD ditemukan pada pasien koinfeksi VHC-HIV yang mencapai SVR dengan terapi Peg-IFN/RBV.