INTISARI

Peningkatan ekspresi VEGF di jaringan hati pada penyakit hati kronik (sirosis hati/SH dan hepatitis kronik) terjadi akibat adanya stimulasi fibroblast dalam pembentukkan jaringan fibrosa. Pada karsinoma hepatoseluler (KHS) peningkaatan ekspresi VEGF terjadi akibat adanya invasi tumor dan metastasis di intrahepatal. Ekspresi VEGF dan reseptor VEGF (VEGFR) di jaringan hati berkorelasi dengan kadarnya di darah. Polimorfisme VEGF (-634;-2578) dan VEGFR jaringan terbukti berpengaruh pada keberhasilan terapi dan pembedahan pada kasus KHS. Belum ada penelitian tentang polimorfisme VEGF-634 dan -2578 serta sVEGFR pada subjek KHS dan penyakit hati kronik.

Penelitian potong lintang dengan consecutive sampling dilakukan pada 183 subjek yang memenuhi kriteria inklusi dan eksklusi (46 KHS, 39 SH, 39 hepatitis kronik dan 59 subjek sehat) di RSUP Dr. Sardjito, Yogyakarta, Indonesia, periode 2010-2013. Pemeriksaan sVEGFR-2 dilakukan pada 149 subjek menggunakan metode ELISA, dan pemeriksaaan sekuensing DNA target VEGF-634 dan -2578 pada 183 subjek menggunakan *Applied Bio stems* (ABI) *chromatography.* Analisis statistik menggunakan *STATA 11.0* dan *openepi version 3.*

Terdapat perbedaan bermakna pada frekuensi genotip VEGF-634 (GG, GC, CC), genotip CC (3,30%) lebih sedikit dibandingkan GC (93,63%) dan GG (23,08%). Terdapat perbedaan bermakana frekuensi alel G dibanding alel C pada subjek hepatitis dan KHS dibandingkan dengan subjek sehat. Terdapat perbedaan bermakna frekuensi genotip VEGF-2578 (CC, CA, AA), genotip AA (8,24%) lebih sedikit dibandingkan CC (42,31%) dan AC (49,45%). Nilai rasio prevalens (RP) >1 VEGF-634 C>G pada subjek: KHS terhadap SH dan hepatitis serta subjek SH dan hepatitis terhadap sehat. Nilai RP>1 VEGF-2578 A>C hanya pada subjek KHS terhadap SH. Polimorfisme lain di sekitar VEGF-2578 yaitu: insersi-delesi (ID) di -2547s/d-2526, delesi di -2549 dan haplotip (Ht) CCGAGCCC, dengan RP>1 pada ID dan Ht subjek SH, hepatitis dan sehat. Terdapat perbedaan bermakna kadar sVEGFR-2 serum pada seluruh subjek, berdasarkan nilai titik potong klinis didapatkan RP>1 pada subjek KHS terhadap SH dan hepatitis, serta SH terhadap hepatitis. Frekuansi alel VEGF -2578 pada subjek KHS berbeda bermakana berdasarkan karakter klinis. Korelasi bermakna antara kadar sVEGFR-2 dengan kriteria klinis pada SH dan hepatitis. Berdasarkan uji multivariat dan kurva ROC-AUC adanya SNP VEGF dan sVEGFR-2 dapat memprediksi kejadian KHS pada subjek SH dan hepatitis, serta kejadian SH pada subjek hepatitis.

Kesimpulan, perbedaan bermakna frekuensi genotip dan alel SNP VEGF (-634;-2578) dan kadar sVEGFR-2 pada subjek KHS, SH, dan hepatitis kronik. SNP -2578 berhubungan dengan kriteria klinis pada KHS, sVEGFR2 berkorelasi pada subjek sirosis dan hepatitis. SNP VEGF (-634;-2578) dan sVEGFR-2 dapat digunakan sebagai prediktor kejadian penyakit KHS dan SH.

Kata kunci: SNP VEGF-634, SNP VEGF-2578, sVEGFR-2, karsinoma hepatoseluler, penyakit hati kronik.

ABSTRACT

Increased of VEGF expression in liver tissue on chronic liver disease (liver cirrhosis/LC and chronic hepatitis) is due to stimulation of fibroblasts in the formation of fibrous tissue. In hepatocellular carcinoma (HCC) that was due to tumor invasion and intrahepatic metastasis. VEGF and tissue VEGFR expression correlated with the levels in blood. VEGF-634 and -2578 polymorphism and VEGFR have been shown as the affects of therapy and surgery in the HCC cases. There has been no research on polymorphism of VEGF-634 and -2578 and sVEGFR in chronic liver disease and HCC.

A cross-sectional study with consecutive sampling included 183 subjects who fulfill the inclusion and exclusion criteria (46 HCC, 39 LC, 39 hepatitis and 59 healthy subjects) in Dr. Sardjito Hospital, Yogyakarta, Indonesia, since 2010 to 2013. SVEGFR-2 examination performed on 149 subjects using ELISA method, and DNA sequencing targets (VEGF-634 and -2578) performed on 183 subjects using Applied Bio stems (ABI) chromatography. Statistical analysis used STATA version 11.0 and OpenEpi 3.

There were significant differences in the genotype frequency of VEGF-634 (GG, GC and CC), CC genotype (3.30%) less than GC (93.63%) and GG (23.08%). There were significant differences in the frequency of allele G than the C allele on HCC and hepatitis subjects compared with healthy. There was a significant difference in the frequency of VEGF-2578 genotype (CC, CA and AA), AA (8.24%) less than the CC (42.31%) and CA (49.45%). Value of prevalence ratio (PR)>1 for VEGF-634 C>G obtained on: HCC to LC and hepatitis, LC and hepatitis to healthy. Value of RP>1 for VEGF-2578 A> C obtained only on HCC to LC. Other VEGF polymorphisms obtained: insertion-deletion (ID) at -2547 until -2526, deletion -2549 and haplotype (Ht) CCGAGCCC, RP>1 for ID and Ht on LC to hepatitis and hepatitis to healthy. Significant differences shown in serum levels of sVEGFR-2 among all subjects, based on the clinical cut off point RP>1 obtained in HCC to LC and hepatitis, and LC to hepatitis. Frequency of genotype -2578 had an association with clinical in HCC subjects and sVEGFR-2 had a correlation with clinical character in LC and CH subjects. Multivariate with ROC-AUC curve analyses obtained for prediction of HCC incidence in LC and hepatitis; and the LC incidence in hepatitis

In conclusion, there were significant differences in the frequency genotype and allele of SNP VEGF-634 and -2578 and sVEGFR-2 levels in subjects KHS, SH, and chronic hepatitis. Genotype of SNP -2578 was associated with clinical character in HCC and sVEGFR-2 was correlated with clinical character in LC and CH. VEGF SNP (-634 and -2578) and serum levels of sVEGFR-2 can be used as predictor disease incidence of HCC and LC.

Keywords: SNP VEGF -634, VEGF SNP -2578, sVEGFR-2, hepatocellular carcinoma, chronic liver disease.